Remarks/Arguments

I. Status of the Claims

Claims 7, 8, 10, 14, and 20-41 were pending when the Final Office Action of December 28, 2005 was mailed to Application. These claims are cancelled, and claims 42-57 are added. Non-limiting support for new claims 42-57 can be found throughout the specification and claims as originally filed. For example, support for "a sequence having at least 95% identity..." in claim 42 can be found at page 7, line 3, of the specification. Thus, no new matter has been entered by way of the instant amendment.

Claims 42-57 are currently pending.

II. Statement of the Substance of the Interview Mailed to Applicants on March 31, 2006

Applicants agree with the Summary of the Interview mailed on March 31, 2006. Applicants also thank the Examiner for this interview.

III. Amendments to the Specification

In the specification, the title has been amended so as to introduce "SCN1A", the elected gene/locus of the present application. Minor clerical errors have been corrected at page 58, line 15 (rat instead of rate). The objected terminology "at the amino acid level" has been removed as requested by the Examiner (see below). SEQ ID NOs have been added in the description, more particularly in the brief description of the drawings in accordance with the Sequence Listing filed on June 5th, 2005, as requested by the Examiner.

Additional support for ^{14}C-guanidine in new claim 51 (similar to former claim 35) can be found for example at page 38, line 2. Support for the "hyperexcitability state" in claim 53 can be found for example at page 59, line 10 and page 17, lines 10-21. Support for "epilepsy with febrile seizures" in claim 44 can be found at page 28, line 29; at page 34, line 9; Example 6, page 54, line 24. No new matter has been added.

Applicants acknowledge and thank the Examiner for the addition of Patrick Cossette and David Ragsdale as inventors in the instant application.

Applicants reserve the right to prosecute the subject matter of the cancelled claims in further applications.

IV. Sequence Listing

While the Examiner states that the "sequence listings filed between 11/24/00 and 6/24/04 have been re-reviewed and found not to contain any new matter in light of Applicant's previous explanations," she raises a new objection under 35 USC 112 for the 2 additional sequence listings filed on January 3, 2005 and June 6, 2005 on the basis that no explanations were provided as to the changes made.

In order to overcome the Examiner's objection, Applicants submit the following clarifications.

1. The sequence listing filed in January 2005 was believed to be identical to the one filed on June 24, 2004. The latter was filed in response to the Office Action dated December 8, 2004, stating that the computer readable form of the earlier-filed sequence listing was unreadable. Thus, the same sequence listing (already filed on June 24, 2004) was resubmitted.

2. The sequence listing filed in June 2005 corrected some errors that were unfortunately found in the previously submitted sequence listing (see 1, above). Indeed, errors occurred during the transfer of the sequence listing from PatentIn Version 2.1 to Version 3.1. The content of the sequence listing filed in June 2005 is thus identical to that filed in January 2005 except that SEQ ID NOs:400-408 were renumbered in order to bring them in line with the sequence listing that was originally filed.

Again, Applicants truly apologize for the confusion relating to the Sequence Listing in the instant case, and believe that everything relating thereto is in order.

In addition, as alluded to above, the Applicants have amended the specification to include sequence identifies as requested by the Examiner.

V. Rejections Under 35 U.S.C. § 132(a) are Overcome

It is alleged that the corrections made at pages 6 and 58 to recite "at the amino acid level" in the amendment of September 17, 2004 introduce new matter.

Applicants disagree with this rejection. However, in view of accelerating the prosecution, the terminology "at the amino acid level," at pages 6 and 58, has been removed. Applicants believe that this rejection has thus been overcome. Applicants submit that this removal should in no way be considered an admission that this clarification was indeed new matter.

VI. Rejections Under 35 U.S.C. § 112 Second Paragraph are Overcome

Claims 7, 8, 10, 14, and 20-41 are found indefinite by the Examiner as she finds unclear whether the claims refer to a compositions or methods.

Applicants disagree with these rejections. However, in an effort to further prosecution, Applicants have cancelled claims 7, 8, 10, 14 and 20-41. In addition the newly presented claims no longer include the terminology "providing a screening assay."

In addition, the Examiner's objection to claim 39 has been rendered moot by the cancellation thereof and the absence of the terminology "blocker" in the newly presented claims.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraw her rejection of claims 7, 8, 10, 14, 20, and 20-41 under 35 U.S.C. § 112, second paragraph.

VII. Rejections Under 35 U.S.C. § 112 First Paragraph are Overcome

A. Written Description

The Action rejects claims 20-23 under 35 USC 112 first paragraph for failing to comply with the written description requirement. It is alleged by the Action that these claims contain new subject matter because the claims recite SEQ ID NOs which are assumed to have been changed in the sequence listings filed in January 2005 and June 2005. Applicants disagree. However, as requested by the Action, Applicants have provided an explanation that indicate that the changes made in these sequence listings are fully supported by the originally filed disclosure dated December 24, 2000. Thus, it should be apparent by the explanation given above that no new matter is present in claims 20-23.

Claims 33-38 are also rejected under 35 USC 112, first paragraph for lack of written description. It is alleged that the terminology "time course of recovery from inactivation" found in claims 33 and 34 as well as the expression "radiolabeled guanidine" in claims 35 and 37 find no support in the description. Applicants disagree. Additionally, in view of the cancellation of claims 33 and 34 and of the replacement of "radiolabeled guanidine" by "^{14}C guanidine" in new claim 51, Applicants submit that the above new matter rejection has been overcome.

Claims 7, 8, 10, 14 and 21 are rejected under 35 USC 112 first paragraph for inadequate written description. Applicants disagree. Additionally, in view of the insertion of sequence identifiers in claim 42, Applicants respectfully submits that this rejection has been rendered moot.

B. Enablement

Claims 7, 8, 10, 14, and 20-41 have also been rejected under 35 USC 112, first paragraph, as allegedly not being enabled for methods of treating "any type of epilepsy" for "selecting a compound for treating", "any human SCN1A". Applicants disagree. The Examiner does agree that the specification is enabling for screening assays comprising composition comprising SEQ ID NO:3 or 4, assaying the activity of a sodium ion channel and selecting a compound that reduces the activity of the sodium ion channel. In view of the amendment to the claims to remove the treatment/therapeutic terminology, the removal of the terminology "neurological disorders" and the insertion of sequence identifiers in claim 42, Applicants respectfully submit that the rejections of claims 7, 8, 10, 14, and 20-41 for a lack of enablement have been overcome.

The newly presented claims, also encompass SCN1A sequences which are highly homologous to those recited in the claimed sequence identifiers ("at least 95%..."). Applicants wish to state that at the time of filing the present application, in view of the teachings thereof and of common general knowledge, functional variants of human SCN1A sodium ion channels as encompassed by (iii) in claim 42, were enabled. Applicants submit a Declaration from Dr. Guy Rouleau, an inventor of the present invention, for support (see Exhibit 1). In view of the above, the foregoing and of the accompanying Declaration, Applicants respectfully request that the Examiner withdraws her rejection for lack of enablement.

Applicants also wish to comment on the Examiner's statement at page 20 that:

> The fact that these mutations are found in some patients with epilepsy but not in controls indicates that these mutations may be associated in some way with epilepsy, however such analysis does not indicate which specific role in SCN1A activity, such mutations affect, or if they alter SCN1A activity in any way."

Final Office Action at 20 (underline added).

Applicants respectfully disagree. The fact that the identification of mutations in SCN1A and their association with epilepsy are statistically significant by definition means that SCN1A activity is involved in epilepsy.

In view of the above and foregoing, the Applicants respectfully request that the Examiner withdraws her rejections of the pending claims under 35 USC 112, first paragraph for lack of enablement or lack of written description.

VIII. Rejections Under 35 U.S.C. § 103 (a) are Overcome

Claims 8, 10, 14, 20, 21, 23-30, 32 and 41 have been rejected under 35 USC 103 (a) as being unpatentable over the combination of Malo and Denyer. The Examiner states "the claims have been broadly interpreted to encompass fragments of SCN1A."

Applicants disagree with the rejections. Applicants agree with the Examiner that Malo does not teach the full length sequences of the present invention or the use of SCN1A proteins for screening compounds that reduce the activity of a human SCN1A channel. Malo teaches a partial sequence of SCN1A. In view of the recitation of claim 42, the partial sequence of Malo is not encompassed by the claim.

The Applicants respectfully submit that the obviousness rejection has been rendered moot. Applicants submit that Denyer does not correct the defect of Malo's partial sequence in its teachings of a use of assays on voltage gated ion channels.

Applicants request that the Examiner withdraws the rejection of claims 8, 10, 14, 20, 21, 23-30, 32 and 41 under 35 USC 103(a).

IX. Conclusions

In view of the pioneering nature of the invention, of the general knowledge of the state of the art and of the above and foregoing, it is respectfully requested that the Examiner withdraw all of the pending rejections and allow the present claims to proceed to issuance.

Respectfully submitted,

Michael R. Krawzsenek
Reg. No. 51,898
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
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Austin, Texas 78701
512.536.3020 (voice)
512.536.4598 (fax)

Date: January 29, 2007

EXHIBIT 1
(Declaration of Guy Rouleau)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	Rouleau *et al.*	Art Unit:	1634
Serial No. :	09/718,355	Examiner :	Jehanne Sitton
Filed :	11/24/2000		
Title :	LOCI FOR IDIOPATHIC GENERALIZED EPILEPSY, MUTATIONS THEREOF AND METHOD USING SAME TO ASSESS, DIAGNOSE, PROGNOSE OR TREAT EPILEPSY		

Mail Stop amendment
Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132 OF GUY ROULEAU TRAVERSING GROUNDS OF REJECTION.

Under 37 C.F.R. § 1.132 and regarding the rejection of claims 33-55, I declare:

1. PROFESSIONAL BACKGROUND

1.1 I, Guy Rouleau, am a researcher and an inventor of the subject matter described and claimed in the above-captioned patent application.

1.2 I am a citizen of Canada, presently residing at 3587 Marlowe, Montréal, Québec, Canada H4A 3L8.

1.3 I received my MD degree (Magna Cum Laude) at the University of Ottawa in 1980 and obtained my Ph.D. (thesis title: Genetic Analysis of Neurofibromatosis Type 2) from Harvard University in Genetics in 1989. Through my education I was also involved in clinical work between 1980-1989 and in research between 1984-1989. In addition, I have been involved in research as early as 1977 and intensively for more than 21 years (1984-present). In particular, since 1989 I have been investigating the genetic basis of human brain tumours, human degenerative diseases and psychiatric illnesses.

1.4 I currently hold the following positions: (1) Tenure Professor in the Faculty of Medicine at the University of Montréal, (2) Adjunct Professor in the Department of Human Genetics at McGill University, and (3) Chair of Canada's Research Chair in Genetics of the Nervous System at the University of Montréal. In addition, I am certified as a specialist of neurology of Québec (1985), a Fellow of the Royal College of Physicians of Canada (1985), and as a specialist of genetics of Québec (1993).

1.6 I have published over 310 peer-reviewed scientific articles in various prestigious journals including: Cell (1), Nature (5), Nature Genetics (12), Science (1), Genomics (28), Proc. Natl. Acad. Sci. (1), Nucl. Acids Res. (8), Am. J. Hum. Genet. (27), Hum. Mol. Genet. (23) and Am. J. Med. Genet. (20), as well as a list of Review Articles, Book Chapters and Presentations as Guest Speaker.

1.7 I have received a number of Honors and Awards, including the Jean-Jacques Lussier Award for the highest standing over the four years of Medical School (1980), The Scientist of the Year Award from the Canadian Broadcasting Corporation (1993), and the Michael Smith Award from the Canadian Institutes of Health Research (2000).

1.8 Please refer to the copy of my *curriculum vitae* in **Appendix A** for more details. Accordingly, I consider that I am well-qualified and sufficiently knowledgeable to comment on neurological diseases such as epilepsy, the genetics of epilepsy and methods of molecular cloning and functional variant analysis of sodium channels.

2. OFFICE ACTION OF DECEMBER 28, 2005

2.1 I have analyzed the final rejection issued by the USPTO for the above-captioned patent application with pending claims 7, 8, 10, 14, and 20-41 directed to screening assays for compounds which reduce the activity of human SCN1A sodium channel. I am a named inventor on the patent application and confirm that I have read and understood the patent application.

2.2 I have also been informed that, based on a telephone interview with the Examiner on March 23, 2006, in which I did not take part, that the Examiner will not allow any forms of variants but plans to restrict the pending claims to the specific sequences disclosed in SEQ ID NOs. 3 and 4, (representing the adult and neonatal forms of the SCN1A protein).

2.3 I intend to provide comments and opinions to demonstrate that a person skilled in the art could, in view of the instant patent application and common general knowledge at the time the patent application was filed, identify functional variants of human SCN1A sodium channels that could be used in accordance with the claimed invention, without recourse to undue experimentation.

3. THE ANALYSIS

3.1 Common general knowledge at the time the application was filed

The human SCN1A sodium channel (as well as other sodium channels) is well-characterized, which allows for the analysis and assessment, both *in silico* and experimental, of the properties of its variants. Inventive steps, such as were necessary for the identification of the items disclosed and claimed in the present invention, would not be required, or undue experimentation needed now, to identify functional variants of this channel to be used as proposed in the patent application. I claim that the common general knowledge on the genetics and biology of sodium channels (regarding conserved domains, sequence alignments, crystallographic structural details, functional assays, etc) at the time of filing of this patent application is sufficient to identify such variants, thus not constituting an invention in itself, but rather a regular experimental approach readily available to persons skilled in the art.

For example, the state of the art can be acknowledged by considering references shown in **Appendix B** [all published prior to Nov 24, 1999]. These references testify to the fact that at the time of filing our provisional patent application, a wealth of information regarding the structure and function of sodium channels was known. In

particular, functionally critical domains and residues had already been identified and widely published for several of these channels, including the SCN1A channel.

In addition, protein sequence alignments of the human SCN1A, SCN2A and SCN3A proteins of the present invention, along with human SCN4A, SCN5A, SCN6A, SCN8A, SCN9A and SCN10A protein sequences that were available prior to filing the provisional patent application in 1999 (**Appendix C**) demonstrate the high level of sequence conservation of the different sodium channel proteins. This high level of conservation allowed us to base the intron/exon structures of the SCN1A, SCN2A and SCN3A genes on that of the SCN4A gene, which at the time was the only sodium channel alpha subunit gene with a published intron/exon structure. More importantly, the high level of sequence conservation allows the skilled artisan cognizant of the sequences of SCN1A, SCN2A and SCN3A to predict functionally critical residues and domains that have been conserved between the different human paralogs of sodium channel alpha subunit proteins.

3.2 Structure/function relationships of sodium channels

A first approach would require the commonly used analysis and comparison of conserved functional domains amongst sodium channels, based on the knowledge available at the time of filing of this application. Functional insights can easily be gained from the perusal of such sequence alignments (**Appendix C**), thus allowing the prediction of an effect on channel function by any given sequence variant. Variants lying within highly conserved domains (see for examples domains I-S6, III-S5 and IV-S6 of **Appendix C**), such as transmembrane sequences involved in channel gating and ion currents are obviously predicted to have deleterious effect on the function of the channel, and can be tested as described below (section 3.3).

Of note, the mutations identified in the present invention map to regions of particular importance in the SCNXA proteins. The Examiner is also referred to the application itself, and in particular to Examples 3, 4, and 5, which teach for example at page 52, starting at line 15:

> "(2) Ser1773Tyr; normal: ATC ATA TcC TTC CTG, patient R9049 (affected with IGE): ATC ATA TmC TTC CTG :(TCC>TAC). **This mutation is in the middle of IV-S6 TM domain;** found in 1/70 IGE patients, and 0/150 control subjects tested. This mutation is interesting from a biological point of view for a number of reasons. First, this region of SCN gene (IV-S6) **has been found to play a critical role in fast inactivation of the SCN, by mutagenesis experiments in rat SCN (McPhee et al., 1998).** This is highly relevant for pathophysiology of epilepsy, since this may increase neuronal hyperexcitability. Moreover, **in patients with GEFs, a mutation has been found in the SCNB1 subunit, causing impairment of the fast inactivation of the SCN (Wallace et al, 1999).** Finally, **many of the antiepileptic drugs (e.g. phenytoin, carbamazepine) primarly act by reducing the repetivive firing of neuron, which also involves fast inactivation of the SCN.**" [emphasis added]

and at page 53, starting at line 15:

> "(2) Leu1768Val, in individuals R8197, R9062 and R9822 (all IGE patients) (found in 3/70 IGE patients and 0/65 control subjects). The mutations is **in the IV-S6 component of the sodium channel, which is important in the inactivation of the channel** (see above for more detail)" [emphasis added]

Of particular note for the Ser1773Tyr mutation was an article published in 1994 by Ragsdale *et al.*, and co-inventor on the corresponding divisional application 10/664,603 (Science 265:1724-1728), in which scanning alanine mutagenesis was used to determine functionally important residues in the IV-S6 domain of the rat SCN2A channel. The sequence conservation is such that both the human and rat SCN1A and SCN2A proteins have identical amino acid sequences for the IV-S6 domain (and the SCN3A protein has only 1 amino acid that is different, see **Appendix C**), allowing extrapolation of functional data from one channel to the other. These researchers identified Phe1764 and Tyr1771 in SCN2A as critically important in modulation of the channel inhibition by the local anesthetic etidocaine, and proposed that these hydrophobic aromatic residues were located in the ion-conducting pore. The Ser1773Tyr mutation in SCN1A identified in an epileptic patient, which is located 1 amino acid N-terminal to the critically important Phe residue mentioned above, would thus be predicted to introduce a

third large hydrophobic aromatic residue within the ion conducting pore and lead to disrupted gating.

3.3 Sodium channel functional assays

The impact of a variant on channel function can be directly assessed using common laboratory techniques, such as the introduction of the sequence variant by site-directed mutagenesis into the cDNA sequence of a cloned sodium channel, followed by functional assays of the channel's properties. Several publications in **Appendix C** use this type of standard analysis to determine the functional significance of conserved residues.

As known in the art, several methods can be used to analyze the structure-function relationship of the variants. For example, one can base this analysis on the over-expression of the variant-bearing cDNAs in either mammalian cells or *Xenopus* oocytes, which allow for the performance of a wide range of channel activity assays, including the methods described and/or enabled in the application and claimed (gating properties, sodium currents, sub-cellular localization, expression levels and processing, post-translational modifications, binding properties, etc). All these are techniques that are well-established and do not, *per se*, constitute an inventive step nor require undue experimentation. Any person skilled in the art could, therefore, use the above-mentioned methods in conjunction with the current general knowledge on sodium channels to predict/determine the functionality of variants, as proposed in the pending claims.

It is noteworthy that Example 6 shows one embodiment of how such structure-function analysis can be carried-out. A residue suspected of being important for function is chosen (D188 in SCN1A, for example). Its location in the protein and its conservation "This amino acid is **conserved in all sodium channels thus far identified, in all species**" (page 55, line 15), reinforces its importance. This residue is also associated with an epilepsy phenotype in an Australian family (mutation D188V). The D188V mutation was thus introduced in rat SCN1A and an oocyte assay used to determine sodium channel function.

> "The amplitude of the currents was dramatically reduced for the mutant. Also, a small shift in the inactivation curve was observed for the mutant, as compared to the wild-type. Taken together, these preliminary results confirm a functional effect of D188V mutation on SCN1A gene. (more detail below)" (page 56, lines 2-6)

The Examiner is also referred to Example 7, which lists numerous other methods and references concerning "Further validation of the role of SCN1A, SCN2A, SCN3A, and specific mutations thereof in IGE and epilepsy in general".

In conclusion, it is my opinion that the identification of variants of the claimed sequences, and a prediction/assessment of their functionality, would not require any inventive step or undue experimentation. We are thus entitled to the variant language found in the pending claims. The teachings contained within the instant patent application combined with the current general knowledge on sodium channels at the time of filing of this application is respectfully submitted to be sufficient to identify such variants without undue experimentation or further invention.

4. CONCLUSION

4.1 All statements of my own knowledge made herein are true and all statements based upon information and belief are believed to be true; furthermore, these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

22/1/07
Date

Dr. Guy Rouleau

APPENDIX A

CURRICULUM VITÆ

Guy A. Rouleau

Table of Content

Identification

Name:	Guy Armand Rouleau
Office Address:	University of Montreal Health Centre Notre-Dame Hospital 1560 Sherbrooke Street East Room Y-3633 Montreal, Quebec Canada H2L 4M1
Home Address: 3587 Marlowe	Montreal, Qc H4A 3L8
Business Phone:	514-890-8000 ext. 24699
Home Phone	514-486-3243
Cell Phone	514-971-4341
Fax:	514-412-7602
E-mail:	guy.rouleau@umontreal.ca
Date of birth:	April 12, 1957
N.A.S.	453 590 457
Citizenship:	Canadian

Education

Medical

University of Ottawa (Magna Cum Laude)	Medicine	M.D.	1976-1980

Graduate

Harvard University	Genetics	Ph.D.	1985-1989

Thesis topic: Genetic Analysis of Neurofibromatosis Type 2

Post-Graduate

Research

Montreal Neurol. Institute	Neuroscience	1984-1985
Massachusetts General Hospital	Neuroscience	1985-1989

Clinical

Montreal General Hospital	Internal Medicine	1980-1982
Montreal Neurological Hospital McGill University	Neurology residency	1982-1985
Massachusetts General Hospital	Clinical and Research Fellow, Neurology	1985-1989

Professional Certification

Certificat de Specialiste au Quebec (Neurologie)	1985
Certified as a Fellow of the Royal College of Physicians of Canada (Neurology)	1985
Certificat de Specialiste au Quebec (Genetique)	1995

Appointments

CHU Sainte-Justine Research Centre	Director	2006-present
Université de Montréal Health Center	Scientific Adjunct Director – Basic research	2005-present
Université de Montréal		
Department of Medicine	Tenured Professor	2004-present
Centre for the Study of Brain Diseases	Creator and Director	2004-present
Canada Research Chair in Genetics of the Nervous System	Chairholder	2004-present

McGill University

Dept. of Human Genetics	Adjunct Professor	2004-present
Dept. of Neurology and Neurosurgery	Professor	1999-2004
Dept. of Neurology and Neurosurgery	Associate Professor	1995-1999
Dept. of Neurology and Neurosurgery	Assistant Professor	1989-1995
Department of Medicine	Professor	1999-2004
Department of Medicine	Associate Professor	1995-1999
Department of Medicine	Assistant Professor	1989-1995
Department of Psychiatry	Cross appointment	1998-Present
Department of Biology	Cross appointment	1992-Present
Department of Human Genetics	Cross appointment	1994-Present
Graham Boeckh Chair for Schizophrenia Research	Director	1998-2004

Special Honours, Awards, Recognition

Year	Name or type	Awarded by
1974	Entrance Scholarship	University of Ottawa
1980	Jean-Jacques Lussier award for highest standing over the four years of medical school.	University of Ottawa
1987	Barbeau Memorial Prize for research in Neuroscience.	Canadian Neurological Society
1993	Scientist of the Year	Societé Radio-Canada
1994	Un des Grands de l'année	Magazine l'Actualité
1999	Prix Leo-Parizeau.	Association Canadienne-Francaise pour l'Avancement de la Science (ACFAS)
2000	Michael Smith Award	Canadian Institutes of Health Research
2000	Award for Professionalism	University of Ottawa, Faculty of Medicine

2000	Prix d'excellence en recherche Merck Frosst	Département de médecine, CUSM
2002	Personnalité de la semaine	La Presse
2005	Prix d'excellence	Département de médecine, UDM

Other Contributions

Journals

Editorial Board

Neurology of Disease	1993 - Present
Canadian Journal of Neurological Sciences	1998 - Present
Annal of Human Genetics	2000 - Present

Ad hoc reviews

Neurology
New England Journal of Medicine
Genomics
American Journal of Human Genetics
Genes, Chromosomes and Cancer
Human Molecular Genetics
Lancet
Neuropsychiatric Genetics
Nature Genetics
Nature
JAMA
Bulletin of the Centre of Excellence for Early Childhood Development

Grant Reviews

Panel Member

Medical Research Council, Genetics Committee	1991-1994.
Amyotrophic Lateral Sclerosis Association of America	1993.
National Neurofibromatosis Foundation,	1995-Pres.
Visite d'évaluation de l'Hôpital St-Luc pour le FRSQ	le 6 février 1996
National Cancer Institute of Canada, Panel B	1997-2000.
National Institute for Health, Ad hoc panels (USA)	1996-Pres.
Canadian Psychiatric Research Foundation,	1999-Pres.
Canadian Institutes of Health Research: Scientific Officer, Genetics Committee,	2000-2003

Chairperson, Genetics Committee, 2003
Pfizer CardioVascular Research Awards
Member of the review committee 2006

Ad hoc reviews

Medical Research Council
Cancer Research Society of Canada
Muscular Dystrophy Association of Canada
Motor Neurone Disease Association (UK)
ALS Society of Canada
National Institutes of Health

Professional and/or Learned societies

Meeting Organizer

Second International Workshop on Chromosome 22 1991
Montebello, Quebec (First Chromosome Specific Workshop held in Canada)

First International Workshop on Oculopharyngeal 1995
Muscular Dystrophy, Quebec, Quebec

Co-organizer Annual Montreal Neurology meeting, May 29-June 1 1997

6th Journées génétiques of the Réseau de médecine génétique 2006
Appliquée of the Fonds de recherche en santé du Québec, Montreal

Member of the supervisory committee International Society 2007
of Adolescent Psychiatry and Psychology, Montréal, July

Examination boards

Vice President, Jury d'examination, Certificat 1991-Present
de Specialiste en Neurologie, Province de Québec.

Membership

Scientific Advisory Board, Généthon, Evry France 1991-Present

Medical and Research Advisory Board 1991-Present
of the National Ataxia Foundation

Member of Human Genome Organization 1992-Present

Member Programme Committee for Genetics and Cell Biology of the Motor Neuron: Third MNDA Sponsored International Conference on MND/ALS	1992
Member of the Institute of Mental Health Research University of Ottawa, Royal Ottawa Hospital	1992-Present
Scientific Advisory Board, Fondation Jean Dausset - CEPH	1998-Present
Member of Scientific Advisory Board of the Centre for Applied Genomics, Hospital for Sick Children	1999-Present
Director of Réseau de Médecine Génétique Avancée - FRSQ	2004-Present
Member of Science Advisory Council (SAC), Neuroscience Canada	2005-present
Member of the Canadian Genomic Mission to Denmark	May 2005
Member of the Advisory Board Canadian Association for Familial Ataxia	2005-Present
Member of the Canadian Academy of Health Sciences	2006-Present

Industrial linkages

Biocapital Inc (Venture Capital fund)

Scientific Advisory Board	1995-2000

RGS Genome

Founder in 1997

Director and Secretary-Treasurer till it's acquisition in Nov. 2000

Xenon Genetics Research Inc. (continuation of RGS Genome Inc. after it's acquisition)

President and Director	2000-2003

Xenon Genetics Inc.

Director	2000-2003
Team Leader for Neuroscience	2000-2003

Conception and organistion of the spin off Emerillon Therapeutics Inc: 2002-2003

Emerillon Therapeutics Inc.

President and Director 2003-Present

Chief Scientific Officer 2003-Present

Bioaxone Inc.

Director 2006-Present

Ad Hoc reviewer for numerous Venture Capital Funds

Research activities

1977	Four months summer studentship from the Muscular Dystrophy Association of Canada to study CPK in the mitochondria of muscle and brown fat of rats.
1984-85	One year investigating the effects of Glucocorticoids on the skeletal muscle of rats.
1985-89	Investigation of neurofibromatosis using molecular biological techniques in the neurogenetics laboratory of the Massachusetts General Hospital.
1989-Present	Investigation of the genetic basis of human brain tumours, human neurodegenerative diseases and psychiatric illnesses.

Supervision

Master Student

Caroline Fournier	Genetic studies of vascular disease	1996-2000
Sean Hayes	Genetic investigation of spinocerebellar ataxia	1996-1999
Faith Au-Yeung	Characterization of the CAG Alanine tract	2002-2005
Linh-An Tuong	Characterization of the CAG Alanine tract	2004-2006
Rob Gillis	Identification of genes associated with autism	2005-
Samar Khoury	Genetic risk factors and sleep disorders in patients with head trauma	2005-
Shawn Stochmanski	Frameshifting in CAG repeat (MGD-3)	2006-

PhD Student

Suzanne Demczuk	Genetic characterization of DiGeorge syndrome	1991-1995

Mohini Lutchman	Cloning and characterization of the NF2 gene	1991-1995
Jaime Claudio	Characterizing the neufibromatosis type 2 gene	1992-1996
Bernard Brais	Genetic studies of oculopharyngeal muscular dystrophy	1992-1997
Iscia Lopes-Cendes	Genetic studies of spino-cerebellar ataxia	1992-1998
Jillian Parboosingh	Mechanism of neurodegeneration	1992-1998
Ronald Lafrenière	Genetic studies of progressive myoclonic epilepsy	1993-1997
Albena Pramatarova	Genetic studies of amyotrophic lateral sclerosis	1993-1999
Marie-Pierre Dubé	Development of new statistical methods for genetic analysis	1994-1999
Gustavo Turecki	Genetic studies of lithium responsive bipolar illness	1994-1999
Ridha Joober	Genetic studies of schizophrenia	1994-1999
Zoha Kibar	Genetic studies of Clouston Hidrotic ectodermal dysplasia	1995-1999
Heidi Howard	Genetic studies of ACCPN	1996-2003
Xueping Fan	Characterization of the OPMD protein	1997-2002
Adriana Diaz	Genetic studies of Tourette's syndrome	1998-2004
Julie Gauthier	Genetic studies of Autism	1999-2005
Inge Meijer	Genetic Analysis of Heriditary Spastic Paraplegia	1998-2006
Francois Gros-Louis	Searching for genes involved in ataxias	2000-2006
Patrick Cossette	Genetics of epilepsy	2000-
Dominique Verlaan	Searching for genes responsible for aneurysm	2001-
Christianne Messaed	Pathogenesis of Oculopharyngeal Muscular Dystrophy	2001-
Anastasia Levchenko	Genetic Analysis of Restless legs syndrome	2002-
Qingling Duan	Genetic susceptibility to engiodema	2002-
Paul Valdmanis	Genetics of ALS	2003-
Adèle Salin	Analyses of ACCPN	2004-
Jean-Baptiste Rivière	Genetic of ACCPN & HSN2	2004-
Ferid Fathalli	The glutamatergic system and schizophrenia	2005-
Matthieu Pasco	Detection and characterization of the response of muscle Cells to polyalanine expansions	2006-

Post-doctoral Fellow

Denise Figlewicz	Genetic studies of ALS	1990-1993
Jun Goto	Genetic studies of ALS	1990-1992
Marc Sanson	Isolating the NF2 gene	1990-1993
Jeff Cochius	Genetics of Epilepsy	1991-1993
Elspeth Twist	Genetics of spinocerebellar ataxia	1992-1994
Martin Ruttledge	Genetics of NF2	1993-1995
Karen Rooke	Genetics of ALS	1994-1995
Youssef Boukaftane	Genetics of ALS	1995-1998
Yagang Xie	Isolating the NF2 protein	1995-1996
Mehrdad Jannatipour	Characterizing the NF2 protein	1996-2001
Vigi Shanmugam	Characterizing the OPMD protein	1997-1999
André Toulouse	Genetic studies of schizophrenia	1997-2003
Collette Hand	Genetic studies of ALS	1998-2002
Patrick Dion	Characterizing OPMD	1997-2004
Nathalie Girard	Molecular Analysis of HSN2	2004-2006
Claudia Gaspar	Characterization of CAG alanine	1999-2006

Aida Abu-Baker	Pathogenesis of OPMD	2000-2006
Lan Xiong	Genetic Study of Schizophrenia	2001-
Nicolas Dupré	Genetic Epidemiology of Ataxias	2001-
Masoud Shekarabi	Pathogenesis of ACCPN, HSN2	2003-
Amélie Piton	Identification of genes predisposing to autism and schizophrenia	2005-
Freya Vercauteren	Dopamine signaling in Restless Legs Syndrome	2006-
Edor Kabashi	Genetics of ALS	2006-
Sébastien Holbert	Models of C.elegans for HSP	2006-
Yoko Oma	Polyalanine expansions and transcriptions	2006-

Publications

Peer-reviewed

1. DesGroseillier JP, Cullen A, **Rouleau GA**. Ambulatory Goeckerman Treatment for Psoriasis. Canadian Medical Association J 1981; 8:1010-1020.

2. Leblanc R, Knowles KF, Melanson D, MacLean JD, **Rouleau GA**, Farmer J-P. Neurocysticercosis: Surgical and Medical Management with Praziquantel. Neurosurgery 1986; 18:419-427.

3. Seizinger BR, **Rouleau GA**, Ozelius L, Lane AH, St. George-Hyslop P, Huson S, Gusella JF and Martuza RL. A Common Pathogenetic Mechanism for Three Different Tumour Types in Bilateral Acoustic Neurofibromatosis. Science 1987; 236:317-319.

4. **Rouleau GA**, Karpati G, Carpenter S, Soza M, Prescott S, Holland P. Glucocorticoid Excess Induces Preferential Depletion of Myosin in Denervated Skeletal Muscle Fibers. J Muscle Nerve 1987; 10:428-438.

5. Seizinger BR, **Rouleau GA**, Ozelius LJ, Lane AH, Faryniarz AG, Chao MV, Huson S, Korf BR, Parry DM, Pericak-Vance MA, Collins FS, Hobbs WJ, Falcone BG, Iannazzi JA, Roy JC, St. George-Hyslop, Tanzi RE, Bothwell, Upadhyaya, Harper P, Goldstein AE, Hoover DL, Bader JL, Spence MA, Mulvihill JJ, Aylsworht AS, Vance JM, Rossenwasser GOD, Gaskell PC, Roses AD, Martuza RL, Breakefield XO, and Gusella JF. Genetic Linkage of Von Recklinghausen Neurofibromatosis to the Nerve Growth Factor receptor gene. Cell 1987; 49:589-594.

6. **Rouleau GA**, Wertelecki W, Haines JL, Hobbs WJ, Trofatter JA, Seizinger B, Martuza RL, Superneau DW, Conneally PM and Gusella JF. Genetic Linkage of Bilateral Acoustic Neurofibromatosis to DNA Markers on Chromosome 22. Nature 1987; 329:246-248.

7. Seizinger BR, **Rouleau GA**, Lane AH, Ozelius LJ, Faryniarz AG, Iannazzi J, Hobbs W, Roy JC, Falcone B, Huson S, Harper P, Parry DM, Bader JL, Spence MA, Gusella JF. DNA Linkage Analysis in von Recklinhausen Neurofibromatosis. J Med Genet 1987; 529-538.

8. Seizinger BR, Martuza RL, **Rouleau GA**, Breakefield XO, Gusella JF. Models for Inherited Susceptibility to Cancer in the Nervous System: A Molecular-Genetic Approach to Neurofibromatosis. Developmental Neuroscience 1987; 9(3):144-153.

9. Seizinger BR, **Rouleau GA**, Lane AH, Farmer G, Ozelius LJ, Haines JL, Parry DM, Korf BR, Pericak-Vance MA, Faryniarz AG et al. Linkage Analysis in Von Recklinghausen Neurofibromatosis (NF1) with DNA Markers for

Chromosome 17. Genomics 1987; 1(4):346-348.

10. Seizinger BR, **Rouleau GA**, Ozelius LJ, Lane AH, Farmer GE, Lamiell JM, Haines J, Yuen JWM, Collins D, Majoor-Krakauer D, Bonner T, Mathew C, Rubenstein A, Halperin J, McConkie-Rosell, Green JS, Trofatter JA, Ponder BA, Eierman L, Bowmer MI, Schimke R, Oostra B, Aronin N, Smith DI, Drabkin H, Waziri MH, Hobbs WJ, Martuza RL, Conneally PM, Hsia YE, Gusella JF. Von Hippel-Lindau Disease is Genetically Linked to the RAF1 Oncogene on Chromosome 3p. Nature 1988; 332:268-269.

11. Wertelecki W, **Rouleau GA**, Superneau DW, Forehand LW, Williams JP, Haines JL, Hobbs WJ, Conneally PM, Gusella JF. Neurofibromatosis-2: Clinical and DNA Linkage Studies of a Large Kindred. New England Journal of Medicine 1988; 319: 278-283.

12. **Rouleau GA**, Kurnit DM, Neve RL, Bazanowsky A, Patterson D, Gusella JF. D22S15 - A Fetal Brain cDNA with BanII and SacI RFLP. Nucleic Acids Research 1988; 16: 1646.

13. **Rouleau GA**, Bazanowski A, Cohen EH, Guellaen G, Gusella JF. Gamma-Glutamyl Transferase Locus (GGT) Displays a PvuII Polymorphism. Nucleic Acids Research 1988; 16:1848.

14. **Rouleau GA**, Haines JL, Bazanowski A, Colella-Crowley A, Trofatter JA, Wexler NS, Conneally PM, Gusella JF. A Genetic Linkage Map of the Long Arm of Human Chromosome 22. Genomics 1989; 4:1-6.

15. Menon AG, Ledbetter D, Rich DC, Seizinger BR, **Rouleau GA**, Michels VF, Schmidt, MA, Dewald G, Dellatorre CM, Haines JL, Gusella JF. Characterization of a Translocation Within the Von Recklinghausen Neurofibromatosis Region of Chromosome 17. Genomics 1989; 5:245-249.

16. El-Azouzi M, Chung RY, Farmer GE, Martuza RL, Black PMcL, **Rouleau GA**, Hettlich C, Hedley-White ET, Zervas NT, Panagopoulos K, Nakamura Y, Gusella JF, Seizinger BR. Loss of Distinct Regions on the Short Arm of Chromosome 17 Associated with Tumorigenesis of Human Astrocytomas. Proc Nat Acad Sci USA 1989; 86 (18):7186-7191.

17. **Rouleau GA**, Seizinger BR, Haines JL, Wertelecki W, Superneau DW, Gusella JF. Flanking Markers Define the Limits of the NF-2 Locus. Am J Hum Genet 1990; 46:323-328.

18. Zhang F, Delattre O, **Rouleau GA**, Couturier J, Lefrancois B, Thomas G, Oriasse A. The Neuroepithelioma Breakpoint on Chromosome 22 is Proximal to the Meningioma Locus. Genomics 1990; 6:174-177.

19. Couturier J, Delattre O, Kujas M, Philippos J, Peter M, **Rouleau GA**, Oriasse A, Thomas G. Assesment of Chromosome 22 Anomalies in Neurinomas by Combined Karyotype and RFLP Analysis. Cytogenetics, Cancer Genetics 1990; 45:55-62.

20. **Rouleau GA**, Bazanowski A, Gusella JF, Haines JL. A Genetic Linkage Map of Chromosome 1: Comparison of Different Data Sets and Linkage Programs. Genomics 1990; 7:313-318.

21. Carey A, Roach S, Williamson R, Dumanski J, Nordenskold M, Collins VP, **Rouleau GA**, Blin N, Jalbeert P, Scambler P. Localisation of 27 DNA Markers to the Region of Human Chromosome 22q11 Deleted in Patients with the DiGeorge Syndrome. Genomics 1990; 7:299-306.

22. Zhang F.R., Aurias A, Delattre O, Stern M.S., Benitez J, **Rouleau GA**, Thomas G. Mapping of Human

Chromosome 22 by In Situ Hybridization. Genomics 1990; 7:319-324.

23. Sanson M, Delattre O, Couturier J, Philippon J, Cophignon J, Derome P, **Rouleau GA**, Thomas G. Parental Origin of Chromosome 22 Alleles Lost in Meningioma. Am J Hum Genet 1990; 47:877-880.

24. Fontaine B, **Rouleau GA**, Seizinger BR, Jewell AF, Hanson MP, Martuza RL, Gusella, JF. Equal Parental Origin of Chromosome 22 Losses in Human Sporadic Meningioma: No Evidence for Genomic Imprinting. Am J Hum Genet 1990; 47:823-827.

25. Jacoby LB, Pulaski K, **Rouleau GA**, Martuza RL. Clonal Analysis of Human Meningiomas and Schwannomas. Cancer Research 1990; 50:6783-6786.

26. Dumanski JP, **Rouleau GA**, Nordenskjold M, Collins VP. Molecular Genetic Analysis of Chromosome 22 in 81 Cases of Meningioma. Cancer Research 1990; 50:5863-5867.

27. Fontaine B, Hanson M, Liou H-C, Glimcher, LH, **Rouleau GA**, Gusella JF. BanI Polymorphism at XBP-1 Locus. Nucleic Acids Research 1990; 18:5578.

28. Fontaine B, Sanson M, Delattre O, Menon AG, **Rouleau GA**, Seizinger BR, Jewell AF, Hanson MP, Aurias A, Martuza RL, Gusella JF, Thomas G. Parental Origin of Chromosome 22 Loss in Sporadic and NF2 Neuromas. Genomics 1991; 10:280-283.

29. Goto J, Figlewicz DA, Lutchman M, Ruddle F, **Rouleau GA**. A PvuII RFLP at the HOX 1.4 Homeobox Locus (HOX1D). Nucleic Acids Research 1991; 19:3755.

30. Siddique T, Figlewicz D, Margaret A, Pericak-Vance M, Haines J, **Rouleau GA**, Jeffers AJ, Sapp P, B.S., Hung W-Y, Bebout J, McKenna-Yasek D, Deng G, Horvitz R, Gusella J, Brown Jr. RH, Allen D, Roses A and collaborators. Linkage of a Gene Causing Familial Amyotrophic Lateral Sclerosis to Chromosome 21 and Evidence for Genetic locus Heterogeneity. New England Journal of Medicine 1991; 324: 1381-1432.

31. Delattre O, Azambuja C, Aurias A, Zucman J, Peter M, Zhang F, Hors-Cayla MC, **Rouleau GA**, Thomas G. Mapping of Human Chromosome 22 with a Panel of Somatic Cell Hybrids. Genomics 1991, 9:721-727.

32. Fontaine B, Trofatter J, **Rouleau GA**, Khurana TS, Haines J, Brown RH Jr., Gusella JF. Different gene loci for hyperkalemic and hypokalemic periodic paralysis. Neuromuscular Disorders 1991; 4:235-238.

33. Aubry M, Marineau C, Zhang F, Zahed L, Figlewicz D, Delattre O, Thomas G, de Jong P, Julien JP, **Rouleau GA**. Cloning of Six New Genes with Zinc Finger Motifs Mapping to Short and Long Arms of Human Acrocentric Chromosome 22. Genomics 1992;13:641-648.

34. Carson WJ, Radvany J, Farrer LA, Vincent D, Rosenberg RN, MacLeod PM, **Rouleau GA**. The Machado-Joseph Disease Locus is Different from the Spinocerebellar Ataxia Locus (SCA1) Genomics 1992; 13:852-855.

35. Narod SA, Parry D, Parboosingh J, Lenoir GM, Ruttledge M, Fischer G, Eldridge R, Martuza R, Frontali M, Haines J, Gusella JF, **Rouleau GA**. Neurofibromatosis Type 2 Appears to be a Genetically Homogeneous Disease. Am J Hum Genet 1992; 51:486-496.

36. Delattre O, Zucman J, Plougastel B, Desmaze C, Melot T, Peter M, Kovar H, Joubert I, de Jong P, **Rouleau GA**,

Aurias A, Thomas G. Gene Fusion With an ETS DNA-Binding Domain Caused by Chromosome Translocation in Human Tumours. Nature 1992; 359:162-165.

37. **Rouleau GA**, Emanuel BS. Proceedings of the Second International Chromosome 22 Workshop. Genomics 1992; 14:1124-1126.

38. Zucman J, Delattre O, Desmaze C, Plougastel B, Joubert I, Melot T, Peter M, De Jong P, **Rouleau GA**, Aurias A, Thomas G. Cloning and Characterization of the Ewing's Sarcoma and Peripheral Neuroepithelioma t(11;22) Translocation Breakpoints. Genes, Chromosomes Cancer 1992; 5:271-277.

39. Tanaka N, Nishisho I, Yamamoto M, Miya A, Shin E, Karakawa K, Fujita S, Kobayashi T, **Rouleau GA**, Mori T, Taki S. Loss of Heterozygosity on the Long Arm of Chromosome 22 in Pheochromocytoma. Genes, Chromosomes Cancer 1992; 5:399-403.

40. Watkins D, **Rouleau GA**. Oncogenes in Glial Tumours. Revue Neurologique 1992; 148:402-407.

41. Zucman J, Delattre O, Desmaze C, Ayambbuya C, **Rouleau GA**, DeJong P, Aurias A, Thomas G. Rapid Isolation of Cosmids from Defined Subregions by Differential Alu-PCR Hybridization on a Chromosome 22 Specific Library. Genomics 1992; 13:395-401.

42. Marineau C, Aubry M, Julien J.-P., **Rouleau GA**. Dinucleotide Repeat Polymorphism at the D22S264 Locus. Nucleic Acids Research 1992; 20:1430.

43. Marineau C, **Rouleau GA**. Dinucleotide Polymorphism at the Human CRYB2 Gene Locus (22q11.2). Nucleic Acids Research 1992; 20:1430.

44. Goto J, Figlewicz DA, Gnirke A, Khodr N, Krizus A, **Rouleau GA**. Dinucleotide Repeat Polymorphism at the D21S219 Locus Which Flanks the GARS-AIRS-GART Gene. Hum Mol Genet 1992; 1:782.

45. Goto J, Figlewicz DA, Marineau C, Khodr N, **Rouleau GA**. Dinucleotide Repeat Polymorphism at the IGF2R Locus. Nucleic Acids Research 1992; 20:923.

46. Goto J, Tassone F, Demczuk S, Gardiner K, Figlewicz DA, Khodr N, **Rouleau GA**. Dinucleotide Repeat Polymorphism at the D21S65 Locus. Nucleic Acids Research 1992; 1:350.

47. Rosen DR, Siddique T, Patterson D, Figlewicz DA, Sapp P, Hentati A, Donaldson D, Goto J, O,Regan JP, Deng H-X, Rahmani Z, Krizus A, McKenna-Yasek D, Cayabyab A, Gaston SM, Berger R, Tanzi RE, Halperin JJ, Herzfeldt B, Van den Bergh R, Hung W-Y, Bird T, Deng G, Mulder DW, Smyth C, Laing NG, Soriano E, Pericak-Vance MP, Haines J, **Rouleau GA**, Gusella JF, Horvitz HR, Brown Jr. RH. Mutations in Cu/Zn Superoxide Dismutase Gene are Associated with Amyotrophic Lateral Sclerosis. Nature 1993; 363:59-62.

48. MacCollin M, Romand D, Budarf M, Denny C, Trofatter J, Menon A, **Rouleau GA**, Fontaine B, Emanuel B, Gusella J. A Set of STS Assays Targeting the Chromosome 22 Physical Framework Markers. Genomics 1993; 15:680-693.

49. **Rouleau GA**, Merel P, Lutchman M, Sanson M, Zucman J, Marineau C, Hoang-Xuan K, Demczuk S, Desmaze C, Plougastel B, Pulst S, Lenoir G, Bijlsma E, Fashold R, Dumanksi J, de Jong P, Parry D, Eldridge R, Aurias A, Delattre O, Thomas G. Alteration in a New Gene Encoding a Putative Membrane Organizing Protein Causes

Neurofibromatosis Type 2. Nature 1993; 363:515-521.

50. Figlewicz DA, Delattre O, Guellaen G, Krizus A, Thomas G, Zucman J, **Rouleau GA**. Mapping of Human Gamma Glutamyl Transpeptidase Genes on Chromosome 22 and Other Human Autosomes. Genomics 1993; 17:299-305.

51. Garofalo O, Figlewicz DA, Leigh PN, Powell JF, Meininger V, Dib M, **Rouleau GA**. Androgen Receptor Gene Polymorphisms in Amyotrophic Lateral Sclerosis. Neuromuscular Disorders 1993; 3:195-199.

52. Goto J, Figlewicz D, Haines J, Brown Jr. R, Khodr N, **Rouleau GA**. The Glycinamide Ribonucleotide Transformylase (GART) Gene is Not Responsible for Familial Amytrophic Lateral Sclerosis. Neuromuscular Disorders 1993; 3:157-160.

53. Sanson M, Marineau C, Lutchman M, Desmaze C, Baron C, Narod S, Delattre O, Lenoir G, Thomas G, Aurias A, **Rouleau GA**. A Germline Deletion in Neurofibromatosis type 2 Supports the Tumor Suppressor Gene Hypothesis. Hum Mol Genet 1993; 8:1215-1220.

54. Simard J, Feunteun J, Lenoir G, Tonin P, Normand T, The V, Vivier A, Lasko D, Morgan K, **Rouleau GA**, Lynch H, Labrie F, Narod SA. Genetic Mapping of the Breast-Ovarian Cancer Syndrome to a Small Interval on Chromosome 17q12-21: Exclusion of Candidate Genes EDH17B2 and RARA. Hum Mol Genet 1993; 8:1193-1199.

55. Rutlledge M.H., Narod SA, Dumanski JP, Parry D, Eldridge R, Wertelecki W, Parboosingh J, Faucher M-C, Lenoir G, Collins VP, Nordenskjold M, **Rouleau GA**. Pre-symptomatic Diagnosis for Neurofibromatosis Type 2 with Chromosome 22 Markers. Neurology 1993; 43:1753-1759.

56. Sanson M, Zhang F, Demczuk S, Delattre O, de Jong P, Aurias A, Thomas G, **Rouleau GA**. Isolation and Mapping of 45 Not1 Linking Clones to Chromosome 22. Genomics 1993; 17:776-779.

57. Fon EA, Demczuk S, Delattre O, Thomas G, **Rouleau GA**. Complete cDNA Sequence and Mapping of the Human Adenylosuccinate Lyase Gene to Chromosome 22q12.1-q13.2. Cytogenetics and Cell Genetics 1993; 64:201-203.

58. Mhatre AN, Trifiro MA, Kazemi-Esfarjani P, Figlewicz DA, **Rouleau GA**, Pinsky L. The Androgen Receptor Derived from the Expanded Trinucleotide Repeat in X-linked Spinal Cord and Bulbar Muscular Atrophy has Reduced Transcriptional Regulatory Competence. Nature Genetics 1993; 5:184-187.

59. Aubry M, Demczuk S, Desmaze C, Aikem M, Aurias A, Julien J.-P., **Rouleau GA**. Isolation of a Zinc Finger Gene Frequently Deleted in DiGeorge Syndrome. Hum Mol Genet 1993; 2:1583-1587.

60. Figlewicz D.A., **Rouleau GA**, Krizus A, Julien J.-P. Polymorphisms in the Multi-Phosphorylation Domain of the Human Heavy Neurofilament Subunit (NEFH) Gene. Gene 1993; 132:297-300.

61. Pulst SM, **Rouleau GA**, Marineau C, Fain P, Sieb J. Familial Meningioma is not Allelic to Neurofibromatosis 2. Neurology 1993; 43:2096-2098.

62. Cochius J, Figlewicz DA, Kalviainen R, Nousianen U, Soderfeldt B, Farrell K, Patay G, Faydman M, Andermann F, Andermann E, **Rouleau GA**. Unverricht-Lundborg Disease: Absence of Non-Allelic Genetic Heterogeneity. Annals of Neurology 1993; 34:739-741.

63. Marineau C, Baron C, Delattre O, Zucman J, Thomas G, **Rouleau GA**. Dinucleotide Repeat Polymorphism at the D22S268 Locus. Hum Mol Genet 1993; 2:336.

64. Goto J, Gnirke A, Khodr N, Kaufer E, Krizus A, Figlewicz DA, **Rouleau GA**. Dinucleotide Repeat Polymorphism at the D21S370 Locus Which Flanks the PRGS (GARS)-PAIS (AIRS)-PGFT (GART) Gene. Hum Mol Genet 1993; 2(5):616.

65. Twist EC, Ruttledge MH, Rousseau M, Papi L, Sanson M, Merel P, Delattre O, Thomas G, **Rouleau GA**. The Neurofibromatosis Type 2 Gene is Inactivated in Schwannomas. Hum Mol Genet 1994; 3:147-151.

66. Claudio JO, Marineau C, **Rouleau GA**. The Mouse Homologue of the Neurofibromatosis Type 2 Gene is Highly Conserved. Hum Mol Genet 1994; 3:185-190.

67. Ruttledge MH, Sarrazin J, Rangaratnam S, Phelan CM, Twist E, Merel P, Delatrre O, Thomas G, Nordenskjold M, Collins VP, Dumanski JP, **Rouleau GA**. Evidence for the Complete Inactivation of the NF2 Gene in the Majority of Sporadic Meningiomas. Nature Genetics 1994; 6:180-184.

68. Watkins D, Dion F, Poisson M, Delattre J-Y, **Rouleau GA**. Analysis of Oncogene Expression in Primary Human Gliomas; Evidence for Increased Expression of the ros Oncogene. Cancer Genetics and Cytogenetics 1994; 72:130-136.

69. Watkins D, **Rouleau GA**. Genetics, Prognosis and Therapy of Central Nervous System Tumors. Cancer Detection and Prevention 1994; 18(2):139-144.

70. Lopes-Cendes I, Andermann E, Attig E, Cendes F, Bosch S, Wagner M, Gerstenbrand F, Andermann F, **Rouleau GA**. Confirmation of the SCA 2 Locus as an Alternative Locus for Dominantly Inherited Spinocerebellar Ataxias and Refinement of the Candidate Region. Am J Hum Genet 1994; 54:774-781.

71. Clarke DB, Farmer JP, Montes J, Watters G, **Rouleau GA**. Newborn Apnea Caused by a Neurofibroma at the Craniocervical Junction. Canadian J Neurological Science 1994; 21:64-66.

72. Claudio JO, Malo D, **Rouleau GA**. The Mouse Neurofibromatosis Type 2 Gene Maps to Chromosome 11. Genomics 1994; 21:437-439.

73. Pramatarova A, Goto J, Nanba E, Nakashima K, Takahashi K, Takagi A, Kanazawa I, Filgewicz D, **Rouleau GA**. A Two Basepair Deletion in the SOD1 Gene Causes Familial Amyotrophic Lateral Sclerosis. Hum Mol Genet 1994; 3:2061-2062.

74. Lopes-Cendes I, Andermann E, **Rouleau GA**. Evidence for the Existence of a Fourth Dominantly Inherited Spinocerebellar Ataxia Locus. Genomics 1994; 21:270-274.

75. Figlewicz DA, Garruto RM, Krizus A, Yanagihara R, **Rouleau GA**. Absence of Mutations in the Cu/Zn Superoxide Dismutase Gene in Amyotrophic Lateral Sclerosis and Parkinsonism-Dementia of Guam. Neurology Report 1994; 5:557-560.

76. Figlewicz DA, Krizus A, Meininger V, Dib M, Klein V, **Rouleau GA**, Julien JP. Variant Alleles of the Neurofilament Heavy Gene Associated with Amyotrophic Lateral Sclerosis. Hum Mol Genet 1994; 3:1757-1761.

77. Figlewicz DA, McInnis MG, Goto J, Haines JL, Warren AC, Krizus A, Khodr N, Brown RH Jr., McKenna-Yasek D, Antonarakis SE, **Rouleau GA**. Identification of Flanking Markers for the Familial Amyotrophic Lateral Sclerosis Gene ALS1 on Chromosome 21. J Neurological Science 1994; 124:90-95.

78. Cochius J, Carpenter S, Andermann E, **Rouleau GA**, Nousiainen U, Kalviainen R, Farrell K, Andermann F. Sweat Gland Vacuoles in Unverricht-Lundborg Disease: A Clue to Diagnosis? Neurology 1994; 44:2372-2375.

79. Thomas G, Delattre O, Zucman J, Merel P, Desmaze C, Melot T, Sanson M, Hoang-Xuan K, Plougastel B, Dejong P, **Rouleau GA**, Aurias A. Genetic Alterations in the Chromosome 22q12 Region Associated with Development of Neuroectodermal Tumours. Cold Spring Harbor Symposia 1994; 555-564.

80. Twist EC, Farrer LA, Radvany J, Macleod PM, Chamberlain S, Rosenberg R, **Rouleau GA**. Machado Joseph Disease is not an Allele of the Spinocerebellar Ataxia 2 Locus (SCA2). Hum Genet 1994; 93:335-338.

81. Demczuk S, Desmaze C, Aikem M, Prieur M, DeDeist F, Sanson M, **Rouleau GA**, Thomas G, Aurias A. Molecular Cytogenetic Analysis of a Series of 23 DiGeorge Syndrome Patients by Fluorescence *in situ* Hybridization. Annals of Genetics. 1994; 37:60-65.

82. Maziade M, Basset AS, Godbout M, Honer WG, Jones B, Kennedy JL, Labelle A, Macciardi F, Martinez M, Merette C, Raymond V, **Rouleau GA**. The National Strategy for Schizophrenia: Genetics. J Psychiatric Neuroscience 1994;19:34-38.

83. Marineau C, Merel P, **Rouleau GA**, Thomas G. Le Gène de la Neurofibromatose de Type 2. Medécine Science 1995; 11:35-42.

84. Twist EC, Casaubon LK, Ruttledge MH, Rao VS, Macleod PM, Radvany J, Zhao Z, Rosenberg RN, Farrer LA, **Rouleau GA**. Machado Joseph Disease Maps to the Same Region of Chromosome 14 as the Spinocerebellar Ataxia Type 3 Locus. Am J Med Genetics 1995; 32:25-31.

85. Brais B, Xie Y-G, Sanson M, Morgan K, Weissenbach J, Korcyn AD, Blumen SC, Fardeau M, Tome F, Bouchard J-P, **Rouleau GA**. The Oculopharyngeal Muscular Dystrophy Locus Maps to the Region of the Cardiac alpha and beta Myosin Heavy Chain Genes on Chromosome 14q11.2-q13. Hum Mol Genet 1995; 4:429-434.

86. Campeau E, Watkins D, **Rouleau GA**, Babul, R, Buchanan JA, Meschino W, Derkaloustian VM. Linkage Analysis in the Nail-Patella Syndrome. Am J Hum Genet 1995; 56:243-247.

87. Demczuk S, Aledo R, Zucman J, Delattre O, Desmaze C, Dauphinot L, Jalbert P, **Rouleau GA**, Thomas G, Aurias. Cloning of a Balanced Translocation Breakpoint in the DiGeorge Syndrome Critical Region and Isolation of a Novel Potential Adhesion Receptor Gene in its Vicinity. Hum Mol Genet 1995; 4:551-558.

88. Maciel P, Gaspar C, DeStefano A, Silveira I, Coutinho P, Radvany J, Dawson D, Sudarsky L, Guimaraes J, Loureiro L, Lopes-Cendes I, Rooke K, Rosenberg R, MacLeod P, Farrer L, Sequeiros J, **Rouleau GA**. Correlation Between CAG Repeat Length and Clinical Features in Machado-Joseph Disease. Am J Hum Genet 1995; 57:54-61.

89. Demczuk S, Levy A, Aubry M, Croquette M.F., Philip N, Prieur M, Sauer U, Bouvagnet P, **Rouleau GA**, Thomas G, Aurias A. Excess of Deletions of Maternal Origin in the DiGeorge/Velo-Cardio-Facial Syndrome. A Study of 22 New Patients and Review of the Literature. Hum Genet 1995; 96:9-13.

90. Lutchman M, **Rouleau GA**. The Neurofibromatosis Type 2 Gene Suppresses Growth of NIH 3T3 Cells. Cancer Research 1995; 55(11); 2270-2274.

91. Parboosingh JS, **Rouleau GA**, Meninger V, McKenna-Yasek D, Brown RH, Figlewicz DA. Absence of Mutations in the Mn Superoxide Dismutase and Catalase Genes in Familial Amyotrophic Lateral Sclerosis. Neuromuscular Disorders 1995; 5:7-10.

92. Pramatarova A, Figlewicz D, Krizus A, Han F, Brown R, Meininger V, **Rouleau GA**. Identification of New Mutations in the Cu/Zn Superoxide Dismutase Gene of Patients with Familial Amyotrophic Lateral Sclerosis. Am J Hum Genet 1995; 56:592-596.

93. Gispert S, Lunkes A, Santos N, Orozco G, Ha-Hao D, Ratzlaff T, Aguiar, Torrens I, Heredero L, Brice A, Cancel G, Stevanin G, Vernant J, Durr A, Lepage-Lezin A, Belal S, Ben-Hamida M, Pulst S, **Rouleau GA**, Weissenbach J, LePasilier D, Kuchertapati R, Montgomery K, Fukui K, Auburger G. Localisation of the Candidate Gene D-Amino Acid Oxidase Outside the Refined 1 CentiMorgan Region of Spinocerebellar Ataxia 2 (SCA2). Am J Hum Genet 1995; 57:972-975.

94. Lafreniere R, De Jong P, **Rouleau GA**. A 405-kb Cosmid Contig and *Hin*dIII Restriction Map of the Progressive Myoclonus Epilepsy Type 1 (EPM1) Candidate Region in 21q22.3. Genomics 1995; 29:288-290.

95. Claudio JO, Lutchman M, **Rouleau GA**. Widespread but Cell Type-Specific Expression of the Mouse Neurofibromatosis Type 2 Gene. NeuroReport 1995; 6:1947-1946.

96. Fon E, Sarrazin J, Meunier C, Alarcia J, Shevell M, Philippe A, Leboyer M, **Rouleau GA**. Adenylosuccinate Lyase (ADSL) and Infantile Autism: Absence of the Previously Reported Point Mutation. Am J Med Genet (Neuropsychiatric Genetics) 1995; 60: 554-557.

97. DeStafano AL, Farrer LA, Maciel P, Gaspar C, **Rouleau GA**, Coutinho P, Sequeiros J. Gender Equality in Machado-Joseph Disease. Nature Genetics 1995; 11:118-119.

98. Mérel P, Hoang-Xuan K, Sanson M, Bijlsma E, **Rouleau GA**, Laurent-Puig P, Pulst S, Baser M, Lenoir G, Sterkers JM, Philippon J, Resche F, Mautner VF, Fischer G, Hulsebos T, Arias A, Delattre O, Thomas G. Screening for Germ-Line Mutations in the NF2 Gene. Genes, Chromosomes & Cancer 1995; 12:117-127.

99. Garofalo O, Figlewicz DA, Thomas SM, Butler R, Lebuis L, **Rouleau GA**, Meininger V, Leigh PN. Superoxide Dismutase Activity in Lymphoblastoid Cells from Motor Neurone Disease/Amyotrophic Lateral Sclerosis (MND/ALS) Patients. J Neurological Science. 1995: 129(S):90-92.

100. Silveira I, Lopes-Cendes I, Kish S, Maciel P, Gaspar C, Coutinho P, Botez MI, Teive H, Arruda W, Steiner CE, Pinto-Junior W, Maciel JA, Jain S, Sack G, Andermann E, Sudarsky L, Rosenberg R, MacLeod P, Chitayat D, Babul R, Sequeiros J, **Rouleau GA**. Frequency of Spinocerebellar Ataxia Type 1, Dentatorubropallidoluysian Atrophy and Machado-Joseph Disease Mutations in a Large Group of Spinocerebellar Patients. Neurology 1995; 46:214-218.

101. Lopes-Cendes I, Phillips HA, Scheffer IE, Mulley JC, Desbiens R, Andermann E, Cendes F, Andermann F, Berkovic S, **Rouleau GA**. Genetic Linkage Studies in Familial Frontal Epilepsy: Exclusion of the Human Chromosome Regions Homologous to the El-1 Mouse Locus. Epilepsy Research 1995; 22:227-233.

102. Beliveau M, Lutchman M, Claudio J, Marineau C, **Rouleau GA**. Schwannomin: New Insights Into This Member of the Band 4.1 Superfamily. Biochemistry and Cell Biology, 1995; 73:733-737.

103. Parboosingh J, Rousseau M, Rogan F, Amit Z, Chetkow H, Johnson W, Manganaro F, Shipper H, Curran T, Stoessl J, **Rouleau GA**. Absence of Mutations in Superoxide Dismutase and Catalase Genes in Patients with Parkinson's Disease. Archives of Neurology 1995; 52:1160-1163.

104. Casaubon L, Melanson M, Lopes-Cendes I, Marineau C, Andermann E, Andermann F, Weissenbach J, Prevost C, Bouchard J.-P., Mathieu J, **Rouleau GA**. The Gene Responsible for a Severe Form of Peripheral Neuropahty and Agenesis of the Corpus Callosum Maps to Chromosome 15q. Am J Hum Genet 1996; 58:28-34.

105. **Rouleau GA**, Clark, A, Rooke K, Pramatarova A, Krizus A, Julien J.-P., Figlewicz D. A Superoxide Dismutase Mutation is Associated with Accumulation of Neurofilaments in Amyotrophic lateral sclerosis. Annals of Neurology 1996; 39:113-117.

106. Rooke K, Figlewicz DA, Han FY, **Rouleau GA**. Analysis of the KSP Repeat of the Neurofilament Heavy Subunit in Familial Amyotrophic Lateral Sclerosis. Neurology 1996; 46:789-790.

107. Lindbald K, Lunkes A, Maciel P, Stevanin G, Zander C, Klockgether T, Ratzlaff T, Brice A, **Rouleau GA**, Hudson T, Auburger G, Schalling M. Mutation Detection in Machado-Joseph Disease Using Repeat Expansion Detection. Molecular Medicine 1996; 2:77-85.

108. Kibar Z, Der Kaloustian V, Brais B, Hani V, Clarke Fraser F, **Rouleau GA**. The Gene Responsible for Clouston Hidrotic Ectodermal Dysplasia Maps to the Pericentromeric Region of Chromsome 13q. Hum Mol Genet 1996; 5:543-547.

109. Ruttledge M, Andermann A, Phelan C, Claudio J, Han F-Y, Chretien N, Rangaratnam S, MacColin M, Short P, Parry, Michels V, Riccardi V, Weksberg R, Kitamura K, Hall B, Propping, **Rouleau GA**. Type of Mutation in the Neurofibromatosis Type 2 Gene (NF2) Frequently Determines Severity of Disease. Am J Hum Genet 1996; 59:331-337.

110. Nechiporuk A, Lopes-Cendes I, Nechiporuk T, Starkman S, Anderman E, **Rouleau GA**, Weissenbach J.S, Pulst S.-M. Genetic Mapping of the Spinocerebellar Ataxia Type 2 Gene on Human Chromosome 12. Neurology 1996; 46:1731-1735.

111. Lopes-Cendes I, Steiner CE, Silveira I, Pinto-Junior W, Maciel J, **Rouleau GA**. Clinical and Molecular Characteristics of a Brazilian Family with Spinocerebellar Ataxia Type 1 (SCA1). Arq. Neuropsiquiatr 1996; 54:412-418.

112. Lutchman M, **Rouleau GA**. Neurofibromatosis Type 2: A new Mechanism of Tumour Suppressor. Trends in Neuroscience 1996; 19:373-377.

113. DeStefano AL, Cupples LA, Maciel P, Gaspar C, Radvany J, Dawson DM, Sudarsky L, Corwin L, Coutinho P, MacLeod P, Sequeiros J, **Rouleau GA**, Farrer LA. A Familial Factor Independent of CAG Repeat Length Influences Age at Onset of Machado-Joseph Disease. Am J Hum Genet 1996; 59:119-127.

114. Lopes-Cendes I, Maciel P, Kish S, Gaspar C, Robitailles Y, Clark B, Koeppen A, Nance M, Schut L, Silveira I,

Coutinho P, Sequeiros J, **Rouleau GA**. Somatic Mosaicism in the Central Nervous Sytem in Spinocerebellar Ataxia Type 1 and Machado-Joseph Disease Patients. Annals of Neurology 1996; 40:199-206.

115. Lopes-Cendes I, Silveira I, Maciel P, Gaspar C, Radvany J, Chitayat D, Babul R, Stewart J, Dolliver M, Robitaille Y, **Rouleau GA**, Sequeiros J. Limits of Clinical Assessment in the Accurate Diagnosis of Machado-Joseph Disease. Archives Neurology 1996; 53:1168-1174.

116. Cavazzoni P, Alda M, Turecki G, **Rouleau GA**, Grof E, Martin R, Duffy A, Grof P. Lithium-Responsive Affective Disorders: No Association With the *tyrosine hydroxylase* Gene. Psychiatry Research 1996; 64:91-96.

117. Lafreniere R, Rochefort D, Kibar Z, Fon E, Han F.-Y, Cochius J, Kang X, Baird S, Korneluk R, Andermann E, Rommens J, **Rouleau GA**. Isolation and Characterization of GT335, a Novel Human Gene Conserved in *Escherichia coli* and Mapping to 21q22.3. Genomics 1996; 38:264-272.

118. Watkins D, Ruttledge M, Sarrazin J, Rangaratnam S, Poisson M, Delattre J.-Y, **Rouleau GA**. Loss of Heterozygosity on Chromosome 22 in Human Gliomas Does not Inactivate the Neurofibromatosis Type 2 Gene. Cancer Genetics and Cytogenetics 1996; 92:73-78.

119. Lafreniere R, Rochefort D, Chretien N, Neville C, Korneluk R, Zuo L, Wei Y, Lichter J, **Rouleau GA**. Isolation and Genomic Structure of a Human Homolog of the Yeast Periodic Tryptophan Protein 2 (PWP2) Gene Mapping to 21q22.3 Genome Research 1996; 6:1216-1226.

120. Turecki G, **Rouleau GA**, Mari JJ, Morgan K. A Systematic Evaluation of Linkage Studies in Bipolar Disorder. Acta Psychiatrica Scandanavia 1996; 93:317-326.

121. Gaspar C, Lopes-Cendes I, DeStefano AL, Maciel P, Silveira I, Coutinho P, MacLeod P, Sequeiros J, Farrer LA, **Rouleau GA**. Linkage Disequilebrium Analysis in Machado-Joseph Disease Patients of Different Ethnic Origins. Hum Genet 1996; 98:620-624.

122. Turecki G, Alda M, Grof P, Grof E, Martin R, Cavazzoni P, Duffy A, Maciel P, **Rouleau GA**. No Association Between Chromosome 18 Markers and Lithium Responsive Affective Disorders. Psychiatry Research 1996; 63:17-23.

123. Turecki G, Grand'Maison F, Lemieux B, **Rouleau GA**. Hyperekplexia and the Alpha Subunit Glycine Receptor Gene (GLRA1). Archives of Neurology 1996; 53:836-837.

124. Pulst S, Nechiporuk A, Neciporuk T, Gispert S, Chen X, lopes-Cendes I, Pearlman S, Starkman S, Orozco-Diez G, Lunkes A, DeJong P, **Rouleau GA**, Auburger G, Korenberg J, Figueroa C, Sahba S. Moderate Expansion of a Normally Biallelic Trinucleotide Repeat in Spinocerebellar Ataxia Type 2. Nature Genetics 1996; 14:269-276.

125. Melanson M, Chalk C, Georgevich L, Fett K, Lapierre Y, Dunong H, Richardson J, Marineau C, **Rouleau GA**. Varicella-zoster Virus DNA in CSF and Arteries in Delayed Contralateral Hemiplegia: Evidence for Viral Invasion of Cerebral Arteries. Neurology 1996; 47:569-570.

126. Joober R, **Rouleau GA**, Fon E, Lal S, Palmour R, Bloom D, Labelle A, Benkelfat C. Apolipoprotein E Genotype in Schizophrenia (letter). Am J Med Genet 1996; 67:235.

127. Fink J, Heiman-Patterson t, Bird T, Cambi F, Dube MP, Figlewicz D, Hentati A, Pericak-Vance M, Raskind W,

Rouleau GA, Siddique T. Hereditary Spastic Paraplegia: Advances in Genetic Research. Hereditary Spastic Paraplegia Working Group. Neurology 1996; 46(6):1731-1735

128. Dubé, M.P., Mlodzienski M, Kibar Z, Farlow M, Eber G, Harper P, Kolodny E, **Rouleau GA**, Figlewicz D. Hereditary Spastic Paraplegia: LOD-Score Consideration for Confirmation of Linkage in a Heterogeneous Trait. Am J Hum Genet 1997; 60:625-629.

129. Lafreniere R, Rochefort D, Chretien N, Rommens J, Cochius J, Kallainen R, Nousiainen U, Patry G, Farrell K, Soderfeld B, Federico A, Hale B, Hernandez-Cossio O, Sorensen T, Pouliot M, Kmiec T, Uldall P, Halasz P, Pranzatelli M, Andermann F, Andermann E, **Rouleau GA**. Unstable Insertion in the 5' Flanking Region of the Cystatin B Gene is the Most Common Mutation in Progressive Myoclonus Epilepsy Type 1 (EPM1). Nature Genetics 1997; 15:298-302.

130. Parboosingh J, Figlewicz D, Krizus A, Meininger V, Azad A, Newman D, **Rouleau GA**. Spinobulbar Muscular Atrophy can Mimic ALS: The Importance of Genetic Testing on Male Patients with Atypical ALS. Neurology 1997; 49:568-572.

131. Goto J, Watanabe M, Ichikawa Y, Yee S, Ihara N, Endo K, Igarashi S, Takiyama Y, Gaspar C, Maciel P, Tsuji S, **Rouleau GA**, Kanazawa I. Machado-Joseph Disease Gene Products Carrying Different Carboxyl Termini. Neuroscience Research 1997; 28:373-377.

132. Maciel P, Lopes-Cendes I, Kish S, Sequeiros J, **Rouleau GA**. Mosaicism of the CAG Repeat in CNS Tissue in Relation ot Age at Death in SCA1 and MJD Patients: Is Glia the Source of Mosaicism in CNS? Am J Hum Genet 1997; 60:993-996.

133. Turecki G, **Rouleau GA**, Joober R, Mari J, Morgan K. Schizophrenia and Chromosome 6p. Am J Med Genet 1997; 74:348-352.

134. Robitaille Y, Lopes-Cendes I, Becher M, **Rouleau GA**, Clark AW. The Neuropathology of CAG Repeat Diseases: Review and Update of Genetic and Molecular Features. Brain Pathology 1997; 7:901-926.

135. Claudio J, Veneziale R, Menko S, **Rouleau GA**. Expression in Schwannomin Lens and Schwann Cells. NeuroReport 1997; 8:2025-2030.

136. Lopes-Cendes I., Teive H., Calcagnotto M., da Costa J., Cardoso F., Maciel J., Radvany J., Arruda W., Trevisol-Bittencourt P., Neto P, Silveira I., Steiner C., Pinto-Junior W., Santos A., Neto Y., Werneck L., Araujo A., Carakushansky G., Mello L., Jardim L., **Rouleau GA**. Frequency of the Different Mutations Causing Spinocerebellar Ataxia in a Large Group of Brazilian Patients. Arq Neuropsiquiatr 1997; 55:519-529.

137. Lafreniere R, Kibar Z, Rochefort D, Han FY, Fon E, Dubé M-P, Kang X, Baird S, Komeluk R, Rommens J, **Rouleau GA**. Genomic Structure of the Human *G7334 (EHOC-1)* Gene Mapping to 21q22.3. Gene 1997; 198:313-321.

138. Saino M, Zhao F, Heiska L, Turunen O, den Bakker M, Zwarthoff E, Lutchman M, **Rouleau GA**, Jääskeläinen J, Vaheri A, Carpen O. Neurofibromatosis 2 Tumor Suppressor Protein Colocalizes with Ezrin and CD44 and Associates with Actin-containing Cytoskeleton. J Cell Science 1997; 110:2249-2260.

139. Lopes-Cendes I, Teive H, Cardoso F, Viana E, Calcagnotto M, da Costa J, Trevisol-Bittencourt P, Maciel J, Rousseau M, Santos A, Araujo A, **Rouleau GA**. Molecular Characteristics of Machado-Joseph Disease

Mutation in 25 Newly Described Brazilian Families. Brazilian J Genet 1997; 20:717-724.

140. Brais B, Bouchard J.-P., Xie YG, Gosselin F, Fardeau M, Tomé F, **Rouleau GA**. Using the Full Power of Linkage Analysis in 11 French Canadian Families to Fine Map the Oculopharyngeal Muscular Dystrophy Gene. Neuromuscular Disorders 1997; 7:S70-S74.

141. Bouchard J.P., Brais B, Brunet D, Gould P, **Rouleau GA**. Recent Studies on Oculopharyngeal Muscular Dystrophy in Quebec. Neuromuscular Disorders 1997; 7:S22-S29.

142. Mathieu J, Lapointe G, Brassard A, Tremblay C, Brais B, **Rouleau GA**, Bouchard J.P. A Pilot Study on Upper Oesophageal Sphincter Dilatation for the Treatment of Dysphagia in Patients with Oculopharyngeal Muscular Dystrophy. Neuromuscular Disorders 1997; 7:S100-S104.

143. Turecki G, **Rouleau GA**, Mari J, Morgan K. Bipolar Disorder and Tyrosine Hydroxylase: a Meta-Analysis. Am J Med Genet 1997; 74:348-352.

144. Turecki G, **Rouleau GA**, Morgan K. Modelling the Phenotype in Parametric Linkage Analysis of Bipolar Disorder. Genetic Epidemiology 1997; 14: 687-691.

145. Shinotoh H, Thiessen B, Snow BJ, Hashimoto S, MacLeod P, Silveira I, **Rouleau GA**, Schulzer M, Calne DB. Fluorodopa and Raclopride PET Analysis of Patients with Machado-Joseph Disease. Neurology 1997; 49: 1133-1136.

146. Brais, B, Bouchard J.P., Xie Y, Rochefort D, Chrétien N, Tomé F, Lafreniere R, Rommens J, Uyama E, Nohira O, Blumen S, Korcyn A, Heutink P, Mathieu J, Duranceau A, Codere F, Fardeau M, **Rouleau GA**. Short GCG expansions in the *PAB2* Gene Cause Oculopharyngeal Muscular Dystrophy. Nature Genetics 1998; 18: 164-167.

148. Sequeiros J, Maciel P, Taborda F, Ledo S, Rocha J, Lopes A, Reto F, Fortuna A, Rousseau M, Fleming M, Coutinho P, **Rouleau GA**, Jorge C. Prenatal Diagnosis of Machado-Joseph Disease by Direct Mutation Analysis. Prenatal Diagnosis 1998; 18:611-617.

149. BoukaftaneY, Khoris J, Moulard B, Salachas F, Meninger V, Malafosse A, Camu W, **Rouleau GA**. Identification of Six Novel SOD1 Gene Mutations in Familial Amyotrophic Lateral Sclerosis Patients. Can J Neurol Sci 1998; 25:192-196.

150. Xie Y, Rochefort D, Brais B, Howard H, Han F, Gou L, Maciel P, Larsson C, **Rouleau GA**. Restriction map of a YAC and cosmid contig encompassing the oculopharyngeal muscular dystrophy candidate region on chromosome 14q11.2-q13. Genomics 1998; 52:201-204.

151. Mohandas N., Hoover K., Tsukita S., Takakuwa Y., Huang S., Arpin M., Benz E., Louvard D, Bretscher A., Tonks N., Ramesch V., Fehon R., Anderson J., Gusella J., Fanning A., Chisti A, Kim A, Mafatia S, Lutchman M, Hanspal M, Jindal H, Chasis J, Liu S, Low P, **Rouleau GA**, Bryant P, Solomon F, Conboy J, Woods D, Gascard P. The FERM Domain: a Unique Module Involved in the Linkage of Cytoplasmic Proteins to the Membrane. Trends in Biochemical Sciences 1998; 23:281-282.

152. Minassian B, Lee J, Herbrick J, Huizenga J, Soder S, Mungall A, Dunham I, Gardner R, Fong CY, Carpenter S, Jardim L, Staishchandra P, Andermann E, Snead O, Lopes-Cendes I, Tsui LC, Delgado-Escueta A, **Rouleau GA**,

Scherer S. Mutations in a Gene Encoding a Novel Protein Tyrosine Phosphatase Cause Progressive Myoclonus Epilepsy. Nature Genetics 1998; 20:171-174.

153. Al-Chalabi A, Andersen PM, Chioza B, Shaw C, Sham PC, Robberecht W, Matthijs G, Camu W, Marklund SL, Forsgren L, **Rouleau GA**, Laing NG, Hurse PV, Siddique T, Leigh PN, Powell JF. Recessive amyotrophic lateral sclerosis families with the D90A *SOD1* mutation share a common founder: evidence for a linked protective factor. Hum Mol Genet 1998; 7:2045-2050.

154. Feit H, Silbergleit A, Schneider LB, Gutierrez JA, Fitoussi R-P, Réyès C, **Rouleau GA**, Brais B, Jackson CE, Beckmann JS, Seboun E. Vocal cord and pharyngeal weakness with autosomal dominant distal myopathy: clinical description and gene localization to 5q31. Am J Hum Genet 1998; 63:1732-1742.

155. Turecki G, **Rouleau GA**, Mari JJ, Joober R, Morgan K. Reply to Bellivier et al. Am J Med Genet 1998; 81:351-352.

156. Turecki G, Grof P, Cavazzoni P, Duffy A, Grof E, Ahrens B, Berghöfer A, Müller-Oerlinghausen B, Dvoráková M, Libigerová E, Vojtechovský M, Zvolský P, Joober R, Nilsson A, Prochazka H, Licht RW, Rasmussen NA, Schou M, Vestergaard P, Holzinger A, Schumann C, Thau K, Rouleau GA, Alda M. Preliminary Evidence for a Role of Phospholipase C-?1 in the Pathogenesis of Bipolar Disorder Responsive to Lithium. Molecular Psychiatry 1998; 3:534-539.

157. Siegel AM, Andermann E, Badhwar A, **Rouleau GA**, Wolford GL, Andermann F, Hess K. Anticipation in familial cavernous angioma: a study of 52 families from International Familial Cavernous Angioma Study. IFCAS Group. Lancet 1998; 352:1676-7.

158. Kish SJ, Lopes-Cendes I, Guttman M, Furukawa Y, Pandolfo M, **Rouleau GA**, Ross B, Nance M, Schut L, Ang L, DiStefano L. Brain glyceraldehyde-3-phosphate dehydrogenase activity in human trinucleotide repeat disorders. Archives of Neurology 1998; 55:1299-1304.

159. Silveira I, Coutinho P, Maciel P, Gaspar C, Hayes S, Dias A, Guimaraes J, Loureiro L, Sequeiros J, **Rouleau GA**. Analysis of SCA1, DRPLA, MJD, SCA2, and SCA6 CAG repeats in 48 Portuguese ataxia families. Am J Med Genet 1998; 81:134-8.

160. Siegel AM, Andermann F, Badhwar A, **Rouleau GA**, Andermann E, Dam M, Hopf H, Dichgans J, Sturzenegger M, Hopf N, Yasui N, Stepper F, Killer M, Vanneste J, Acciarri N, Drigo P, Christensen J, Braun V, Konu D, Andermann E. Anticipation in familial cavernous angioma: ascertainment bias or genetic cause. Acta Neurologica Scandinavica 1998; 98:372-6.

161. Joober R, Benkelfat C, Jannatipour M, Turecki G, Lal S, Mandel J, Bloom D, Lalonde P, Lopes-Cendes I, Fortin D, **Rouleau GA**. Polyglutamine-containing proteins in schizophrenia. Molecular Psychiatry 1999; 4:53-57.

162. Joober R, Benkelfat C, Brisebois K, Lafreniere R, Turecki G, Lal S, Bloom D, Labelle A, Lalonde P, Fortin D, Alda M, Morgan K, Palmour R, **Rouleau GA**. Lack of Association between the hSKCa3 Channel Gene CAG Polymorphism and Schizophrenia. Am J Med Genet 1999; 88:154-157.

163. Kibar Z, Lafreniere R, Chakravarti A, Wang J, Chevrette M, Der Kaloustian V, **Rouleau GA**. A Radiation Hybrid Map of 48 Loci Including the Clouston Hidrotic Ectodermal Dysplasia (HED) Locus in the Pericentromeric Region of Chromosome 13q. Genomics 1999; 56:127-130.

164. Joober R, Benkelfat C, Brisebois K, Toulouse A, Turecki G, Lal S, Bloom D, Labelle A, Lalonde P, Fortin D, Alda M, Palmour R, **Rouleau GA**. T102C polymorphism in the $5HT_{2A}$ gene and schizophrenia: relation to phenotype and drug response variability. J Psychiatry and Neuroscience 1999; 24:141-146.

165. Mezei M, Mankodi A, Brais B, Marineau C, Thornton C, **Rouleau GA**, Karpati G. Subclinical (GCG) Trinucleotide Expansion in the *PABP2* Gene is Not a Predisposing Genetic Factor for Sporadic Inclusion Body Myositis. Neurology 1999; 52:669-670.

166. Maciel P, Gaspar C, Guimaraes L, Goto J, Lopes-Cendes I, Hayes S, Arvidsson K, Dias A, Sequeiros J, Sousa A, **Rouleau GA**. Study of Three Intragenic Polymorphisms in the Machado-Joseph Disease Gene (MJD1) in Relation to Genetic Instability of the $(CAG)_n$ Tract. Eur J Hum Genet 1999; 7:147-156.

167. Brais B, **Rouleau GA**, Bouchard J-P, Fardeau M, Tomé FMS. Oculopharyngeal Muscular Dystrophy. Seminars in Neurology 1999; 19:59-66.

168. Dichgans M, Schols L, Herzog J, Stevanin G, Weirich-Schwaiger H, **Rouleau GA**, Burk K, Klockgether T, Zuhlke C, Laccone F, Riess O, Gasser T. Spinocerebellar Ataxia type 6: evidence for a strong Founder Effect among German families. Neurology 1999; 52:849-51.

169. Blumen SC, Brais B, Korczyn AD, Medinsky S, Chapman J, Asherov A, Nisipeanu P, Codere F, Bouchard JP, Fardeau M, Tome FM, **Rouleau GA**. Homozygotes for Oculopharyngeal Muscular Dystrophy have a Severe form of the Disease. Annals of Neurology 1999; 46:115-8.

170. Mackay D, Ionides A, Kibar Z, **Rouleau GA**, Berryl V, Moore A, Shiels A, Bhattacharya S. Connexin-46 mutations in autosomal dominant congenital cataract. Am J Hum Genet 1999; 64:1357-64.

171. Turecki G, Grof P, Cavazzoni P, Duffy A, Grof E, Ahrens B, Berghöfer A, Müller-Oerlinghausen B, Dvoráková M, Libigerová E, Vojtechovský M, Zvolský P, Joober R, Nilsson A, Prochazka H, Licht RW, Rasmussen NA, Schou M, Vestergaard P, Holzinger A, Schumann C, Thau K, **Rouleau GA**, Alda M. - MAOA: Association and linkage studies in lithium responsive bipolar disorder. Psychiatric Genet 1999; 9:13-16.

172. Turecki G, Brière R, Dewar K, Antonetti T, Lesage A, Séguin M, Chawky N, Alda M, Joober R, Benkelfat C, **Rouleau GA**. Prediction of level of serotonin 2A receptor binding by serotonin receptor 2A genetic variation in postmortem brain samples from subjects who did or did not commit suicide. Am J Psychiatry 1999; 156:1456-1458.

173. Turecki G, Alda M, Grof P, Cavazzoni P, Duffy A, Grof E, Ahrens B, Berghöfer A, Müller-Oerlinghausen B, Dvoráková M, Libigerová E, Vojtechovský M, Zvolský P, Joober R, Nilsson A, Prochazka H, Licht RW, Rasmussen NA, Schou M, Vestergaard P, Holzinger A, Schumann C, Thau K, **Rouleau GA**. Polyglutamine tracts: No evidence of a major role in bipolar disorder. Mol Psychiatry, 1999; 4:220-221

174. Parboosingh JS, Meininger V, McKenna-Yasek D, Brown RH, **Rouleau GA**. Deletions causing spinal muscular atrophy do not predispose to amyotrophic lateral sclerosis. Archives of Neurology 1999; 56:710-712.

175. Larson GP, Ding S, Lafrenière RG, **Rouleau GA**, Krontiris TG. Instability of the EPM1 minisatellite. Hum Mol Genet 1999; 8:1985-1988.

176. Camu W, Khoris J, Moulard B, Salachas F, Briolotti V, **Rouleau GA**, Meininger V. Genetics of familial ALS and

consequences for diagnosis. French ALS Research Group. J Neurological Sciences 1999; 165 Suppl 1:S21-6.

177. Joober R, Benkelfat C, Toulouse A, Lafreniere RGA, Lal S, Ajroud S, Turecki G, Bloom D, Labelle A, Lalonde P, Alda M, Morgan K, Palmour R, **Rouleau GA**. Analysis of 14 CAG-repeat containing genes in Schizophrenia. Am J Med Genet 1999; 88:694-699.

178. Turecki G, **Rouleau GA**, Alda M. Family Density of Alcoholism and Linkage Information in the Analysis of COGA data. Genetic Epidemiology 1999; 17:S361-366.

179. Turecki G, Grof P, Cavazzoni P, Duffy A, Grof E, Martin R, Joober R, Rouleau GA, Alda M. Lithium responsive bipolar disorder, unilineality and chromosome 18: a linkage study. Am J Med Genet 1999; 88:411-415.

180. Lopes-Cendes I, Scheffer IE, Berkovic SF, Rousseau M, Andermann E, **Rouleau GA**. A New Locus for Idiopathic Generalized Epilepsy Maps to Chromosome 2. Am J Hum Genet. 2000 66:698-701.

181. Khoris J, Moulard B, Briolotti V, Hayer M, Durieux A, Clavelou P, Malafosse A, **Rouleau GA**, Camu W. Coexistence of dominant and recessive familial amyotrophic lateral sclerosis with the D90A Cu,Zn superoxide dismutase mutation within the same country. Eur J Neurol 2000 7:207-211.

182. Legoix P, Der Sarkissian H, Cazes L, Giraud S, Sor F, **Rouleau GA**, Lenoir G, Thomas G, Zucman-Rossi J. Molecular characterization of germline NF2 gene rearrangements. Genomics 2000, 65:62-66.

183. Turecki G, Alda M, Grof P, Cavazzoni P, Duffy A, Grof E, Lafrenière R, Joober R, Ahrens B, Berghöfer A, Müller-Oerlinghausen B, Dvořáková M, Libigerová E, Vojtechovský M, Zvolský P, Nilsson A, Prochazka H, Licht RW, Rasmussen NA, Schou M, Vestergaard P, Holzinger A, Schumann C, Thau K, **Rouleau GA**, Polyglutamine coding genes in bipolar disorder: investigation of selected candidate loci. J Aff Disor 2000, 58:63-8

184. Ross BM, Eder K, Moszczynska A, Mamalias N, Lamarche J, Ang L, Pandolfo M, **Rouleau GA**, Kirchgessner M, Kish SJ. Abnormal activity of membrane phospholipid synthetic enzymes in the brain of patients with Friedreich's ataxia and spinocerebellar atrophy type-1. Movement Disorders 2000, 15:294-300.

185. Furakawa Y, Guttman M, Sparagana SP, Trugman J, Hyland K, Wyatt P, Land AE, **Rouleau GA**, Shimadzu M, Kish SJ. Dopa-responsive dystonia due to a large deletion in the GTP cyclohydrozylase I gene. Annals of Neurology 2000, 47:517-520.

186. Lamartine J, Laoudj D, Blanchet-Bardon C, Kibar Z, Soularue P, Ridoux V, Dubertret L, **Rouleau GA**, Waksman G. Refined localization of the gene for Clouston Syndrome (Hidrotic Ectodermal Dysplasia) in a large French family. British J Dermatology, 2000; 142:248-242.

187. Hayes S, Turecki G, Brisebois K, Lopes-Cendes I, Gaspar C, Riess O, Ranum LPW, Pulst S-M, **Rouleau GA**. CAG repeat length in *RAI1* is associated with age at onset variability in spinocerebellar ataxia type 2 (SCA2). Hum Mol Genet 2000; 9:1753-1758.

188. Kibar Z, Dubé M-P, Powel J, McCuaig, Zonana J, Hayflick SJ, Hovnanian A, Radhakrishna U, Antonarakis SE, Benohanian A, Sheeran AD, Stephan ML, Gosselin R, Kelsell DP, Christianson AL, Fraser FC, Der Kaloustian VM, **Rouleau GA**. Clouston hidrotic ectodermal dysplasia (HED): genetic homogeneity, presence of a founder effect in the French-Canadian population and fine genetic mapping. Eur J Hum Genet 2000; 8:372-380.

189. Lamartine J, Pitaval A, Soularue P, Lanneluc I, Lemaitre G, Kibar Z, **Rouleau GA**, Waksman G. A 1.5-Mb physical map of the hidrotic ectodermal dysplasia (Clouston syndrome) gene region on human chromosome 13q11. Genomics, *2000*; 67:232-236.

190. Joober R, Benkelfat C, Lal S, Bloom D, Labelle A, Lalonde P, Turecki G, Rozen R, **Rouleau GA**. Association between the methylenetetrahydrofolate reductase 677C→T missense mutation and schizophrenia. Mol Psychiatry, *2000*; 5:323-326.

191. Alda M, Turecki G, Grof P, Cavazzoni P, Duffy A, Grof E, Lafrenière R, Ahrens B, Berghöfer A, Müller-Oerlinghausen B, Dvoráková M, Libigerová E, Vojtechovský M, Zvolský P, Nilsson A, Prochazka H, Licht RW, Rasmussen NA, Schou M, Vestergaard P, Holzinger A, Schumann C, Thau K, **Rouleau GA**, Association and linkage studies of CRH and PENK genes in bipolar disorder: a collaborative IGSLI study. Am J Med Genet, *2000*; 96:178-181.

192. Minassian BA, Ianzano L, Meloche M, Andermann E, **Rouleau GA**, Delgado-Escueda AV, Scherer SW. Mutation spectrum and predicted function of laforin in Lafora's progressive myoclonus epilepsy. Neurology, *2000*;55:341-346.

193. Joober R, Toulouse A, Benkelfat C, Lal S, Bloom D, Labelle A, Lalonde P, Turecki G, **Rouleau GA**. DRD3 and DAT1 genes in schizophrenia: an association study. J Psychiatr Res *2000*; 34:285-291.

194. Calado A, Tome FM, Brais B, **Rouleau GA**, Kuhn U, Wahle E, Carmo-Fonseca M. Nuclear inclusions in the oculopharyngeal muscular dystrophy consist of Poly(A) binding protein 2 aggregates which sequester poly(A) RNA. Hum Mol Genet *2000*:9:2321-2328.

195. Shanmugam V, Dion P, Rochefort D, Laganiere J, Brais B, **Rouleau GA**. PABP2 polyalanine tract expansion causes intranuclear inclusions in oculopharyngeal muscular dystrophy. Annals Neurology, *2000*; 48:798-802

196. Gaspar C, Jannatipour M, Dion P, Laganiere J, Sequeiros J, Brais B, **Rouleau GA**. CAG tract of MJD-1 maybe prone to frameshifts causing polyalanine accumulation. Hum Mol Genet *2000*; 9:1957-66.

197. Denghien I, Joober R, **Rouleau GA**, Néri C. Polyglutamine tracts in schizophrenia: gaining new insigths. Mol Psychiatry *2000*; 5:236-7.

198. Lamartine J, Essenfelder GM, Kibar Z, Lanneluc I, Callouet E, Laoudj D, Lemaître G, Hand C, Hayflick SJ, Zonana J, Antonorakis S, Kelsell DP, Christianson AL, Pitaval A, Der Kaloustian V, Fraser C, Blanchet-Bardon C, **Rouleau GA**, Waksman G. Mutations in GJB6 cause hidrotic ectodermal dysplasia. Nature Genetics *2000*; 26:142-144.

199. Blumen SC, Korczyn AD, Lavoie H, Medynski S, Chapman J, Asherov A, Nisipeanu P, Carasso RL, Bouchard JP, Tome FMS, **Rouleau GA**, Brais B. Oculopharyngeal Muscular Dystrophy among Bukhara Jews is due to an old Founder Effect producing the $(GCG)_8$ expansion in the PABP2 gene. Neurology, *2000*; 55:12676-1270.

200. Turecki G, Brière R, Dewar K, Lesage A, Séguin M, Chawky N, Vanier C, Alda M; Joober R; Benkelfat C; **Rouleau GA**. Dr. Turecki and colleagues reply. Am J Psychiatry *2000*; 1710-1711.

201. Duffy A, Turecki G, Grof P, Cavazzoni P, Grof E, Lafreniére R, Ahrens B, Berghöfer A, Müller-Oerlinghausen B, Dvoráková M, Libigerová E, Vojtechovský M, Zvolský P, Nilsson A, Prochazka H, Licht RW, Rasmussen NA,

Schou M, Vestergaard P, Holzinger A, Schumann C, Thau K, **Rouleau GA**, Alda M. Association and Linkage Studies of Candidate Genes Involved in GABAergic Neurotransmission in Lithium Responsive Bipolar Disorder. J Psychiatry Neurosci. 2000;25:353-358.

202.Davenport WJ, Siegel AM, Dichgans J, Drigo P, Mammi I, Pereda P, Wood NW, **Rouleau GA**. *CCM1* mutations in families segregating cerebral cavernous malformations. Neurology 2001; 56:540-543.

203.Turecki G, Brière R, Dewar K, Lesage A, Séguin M, Chawky N, Vanier C, Alda M; Joober R; Benkelfat C; **Rouleau GA**. Reply to Harrison. Am J Psychiatry 2001; 158:148.

204.Turecki G, Zhu Z, Tzenova J, Lesage A, Séguin M, Tousignant M, Chawky N, Vanier C, Lipp O, Alda M, Joober R, Benkelfat C, **Rouleau GA**. TPH and Suicidal Behavior: A Study in Suicide Completers. Mol Psychiatry. 2001;698-102.

205.Dupré N, Cossette L, Hand CK, Bouchard J-P, **Rouleau GA**, Puymirat J. A Founder Mutation in French-Canadian Families with X-linked Hereditary Neuropathy. Can J Neuroscience. 2001; 38:51-55.

206.Hadano S, Yanagisawa Y, Skaug J, Fichter K, Nasir J, Martindale D, Koop BF, Scherer SW, Nicholson DW, **Rouleau GA**, Ikeda JE, Hayden MR. Cloning and Characterization of three Novel Genes, ALS2CR1, ALS2CR2 and ALS2CR3, in the Juvenile Amyotrophic Lateral Sclerosis (ALS2) Critical Region at Chromosome 2q33-q34: Candidate Genes for ALS2. Genomics 2001; 71:200-213.

207.Bruder CE, Hirvela C, Tapia-Paez I, Fransson I, Segraves R, Hamilton G, Zhang X, Evans E, Baser M, Zucman-Rossi J, Hergersberg M, Boltshauser E, Papi L, **Rouleau GA**, Poptodorov G, Jordanova A, Kluwe L, Mautner V, Saino M, Hung G, Mathiesen T, Moller C, Pulst S, Harder H, Hellber A, Hondo M, Sahlen S, Blennow E, Albertson D, Pinkel D, Dumanski J. High Resolution Deletion Analysis of Constitutional DNA from Neurofibromatosis type 2 (NF2) Patients Using Microarray-CGH. Hum Mol Genet 2001; 10:271-282.

208.Kotorii S, Takahashi K, Kamimura K, Nishio T, Arima K, Yamada H, Uyama E, Uchino M, Suenaga A, Matsumoto M, Kuchel G, **Rouleau GA**, Tabira T. Mutations of the Notch3 Gene in Non-Caucasian Patients with Suspected CADASIL Syndrome. Dement Geriatr Cogn Disord 2001; 12:185-193.

209.Gaspar C, Lopes-Cendes I, Hayes S, Goto J, Arvidsson K, Dias A, Silveira I, Maciel P, Coutinho P, Lima M, Zhou YX, Soong BW, Watanabe M, Giunti P, Stevanin G, Riess O, Sasaki H, Hsieh M, Nicholson GA, Brunt E, Higgins JJ, Lauritzen M, Tranebjaerg L, Volpini V, Wood N, Ranum L, Tsuji S, Brice A, Sequeiros J, **Rouleau GA**. Ancestral Origins of the Machado-Josheph Disease Mutation: A Worldwide Haplotype Study. Am J Hum Genet 2001; 68:523-528.

210.Hand C, Mayeux-Portas V, Khoris J, Briolotti V, Clavelou P, Camu W, **Rouleau GA**. Compound Heterozygous D90A and D96N SOD1 Mutations in a Recessive Amyotrophic Lateral Sclerosis Family. Annals of Neurology 2001; 49:267-271.

211.Fortin A, Diez E, Rochefort D, Laroche L, Malo D, **Rouleau GA**, Gros P, Skamene E. Recombinant Congenic Strains Derived from A/J and C57BL/6J: A Tool for Genetic Dissection of Complex Traits. Genomics 2001; 74:21-35.

212.Alda M, Keller D, Grof E, Turecki G, Cavazzoni P, Duffy A, **Rouleau GA**, Grof P, Young T. Is Lithium Response Related To Gs? Levels in Transformed Lymphoblasts from Subjects with Bipolar Disorder? J Affect Disord 2001;

65:117-22.

213.Ftouhi-Paquin N, Alda M, Grof P, Chretien N, **Rouleau GA**, Turecki G. Identification of three polymorphisms in the translated region of PLC-gamma1 and their investigation in lithium responsive bipolar disorder. Am J Med Genet 2001; 105:301-5.

214.Fitch D, Lesage A, Seguin M, Trousignant M, Bankelfat C, **Rouleau GA**, Turecki G. Suicide and the serotonin transporter gene. Mol Psychiatry 2001; 6:127-8.

215.Yamamoto K, Bloom D, La S, Turecki G, Joober R, Benkelfat C, Lalonde P, Labelle A, **Rouleau GA**. Polymorphism in the cell division cycle 45 like gene and schizophrenia. Am J Med Genet 2001; 105:214-5.

216.Pramatarova A, Laganière L, Roussel J, Brisebois K, **Rouleau GA**. Neuron specific expression of mutant SOD1 in transgenic mice does not lead to motor impairment. J Neuroscience 2001; 21:3369-74.

217.LaRow JA, Mysliborski J, Rappaport IP, **Rouleau GA**, Carlson, JA. Alopecia areata universalis in an infant. J Qual Med Surg 2001; 5:131-4.

218.Ichikawa Y, Goto J, Hattori M, Toyoda A, Ishii K, Jeong S-Y, Hashida H, Masuda N, Ogata K, Kasai F, Hirai M, Macial P, **Rouleau GA**, Sakaki Y, Kanazawa I. The genomic structure and expression of MJD, the Machado-Joseph disease gene. J Hum Genet 2001; 46:413-422.

219.Nikpoor B, Turecki G, Fournier C, Theroux P, **Rouleau GA**. A Functional Myeloperoxidase Polymorphic Variant is associated ith Coronary Artery Disease in French Canadians. Am Heart J 2001; 142:336-339.

220.Jannatipour M, Dion P, Khan S, Jindal H, Fan X, Laganière J, Chishti AH, **Rouleau GA**. Schwannomin isoform-1 interacts with syntenin via PDZ domians. J Biol Chem 2001; 276:33,093-33,100.

221.Turecki G, Grof P, Grof E, D'Souza V, Lebuis L, Marineau C, Cavazzoni P, Duffy A, Betard C, Zvolsky P, Robertson C, Brewer C, Hudson TJ, **Rouleau GA**, Alda M. Mapping susceptibility genes for bipolar disorder: a pharmacogenetic approach based on excellent response to lithium. Mol Psychiatry 2001; 6:570-8.

222.Hadano S, Hand CK, Osuga H, Yanagisawa Y, Otomo A, Devon RS, Miyamoto N, Showguchi-Miyata J, Okada Y, Singaraja R, Figlewicz DA, Kwiatkowski T, Hosler BA, Sagie T, Skaug J, Nasir J, Brown RH, Scherer SW, **Rouleau GA**, Hayden MR & Ikeda J-E. A gene encoding a putative GTPase regulator is mutated in familial amyotrophic lateral sclerosis 2. Nature Genetics 2001; 29:166-173.

223.Desautels A, Turecki G, Montplaisir J, Ftouhi-Paquin N, Michaud M, Chouinard V-A, **Rouleau GA**. Dopaminergic neurotransmission and restless legs syndrome: A genetic association analysis. Neurology 2001; 57(7):1304-1306.

224.Chambers DM, **Rouleau GA**, Abbott CM. Comparative genomic analysis of genes encoding translation elongation factor 1bα in human and mouse shows eef1b1 to be a retrotransposition event. Genomics 2001; 77:145-148.

225.Fan X, Dion P, Laganiere J, Brais B, **Rouleau GA**. Oligomerization of polyalanine expanded PABPN1 facilitates nuclear protein aggregation that is associated with cell death. Hum Mol Genet 2001;10:2341-2351.

226.Desautels A, Turecki G, Montplaisir J, Sequeira A, Verner A, **Rouleau GA**. Identification of a major susceptibility

locus for restless legs syndrome on chromosome 12q. Am J Hum Genet 2001;69(6):1266-1270.

227.Maciel P, Costa MC, Ferro A, Rousseau M, Santos CS, Gaspar C, Barros J, **Rouleau GA**, Coutinho P, Sequeiros J. Improvement in the molecular diagnosis of Machado-Joseph disease. Arch Neurol 2001; 58:1821-1827.

228.Codere F, Brais B, **Rouleau GA**, Lafontaine E. Oculopharyngeal muscular dystrophy: What's new? Orbit 2001; 20(4):259-266

229.Hand CK, Khoris J, Salachas F, Gros-Louis F, Simoes Lopes AA, Mayeux-Portas V, Brown RH, Meininger V, Camu W, **Rouleau GA**. A novel locus for familial amyotrophic lateral sclerosis, on chromosome 18q. Am J Hum Genet 2002; 70:251-256.

230.Hand CK, **Rouleau GA**. Familial Amyotrophic Lateral Sclerosis. Muscle and Nerve 2002; 25:135-159.

231.Meijer I, Hand CK, Cossette P, Figlewicz DA, **Rouleau GA**. Spectrum of SPG4 mutations in a large collection on North American families with Hereditary Spastic Paraplegia. Arch Neurol 2002: 59:281-286.

232.Meijer I, Hand CK, Grewal KK, Stefanelli MG, Ives EJ, **Rouleau GA**. A locus for autosomal dominant Hereditary Spastic Ataxia, SAX1, maps to Chromosome 12p13. Am J Hum Genet 2002; 70:763-769.

233.Joober R, **Rouleau GA**, Lal S, Dixon M, O'Driscoll G, Palmour R, Annable L, Bloom D, Lalonde P, Labelle A, Benkelfat C. Neuropsychological impairments in neuroleptic-responder vs. –nonresponder schizophrenic patients and healthy volunteers. Schizophr Res 2002; 53:229-238.

234.Verlaan DJ, Davenport WJ, Stefan H, Sure U, Siegel AM, **Rouleau GA**. Cerebral cavernous malformations: Mutations in Krit1. Neurology 2002; 58:853-7

235.Verlaan DJ, Siegel AM, **Rouleau GA**. Krit1 missense mutations lead to splicing errors in cerebral cavernous malformation (CCM). Am J Hum Genet 2002; 70:1564-7

236.Cossette P, Liu L, Brisebois K, Dong H, Lortie A, Vanasse M, Saint-Hilaire JM, Carmant L, Verner A, Lu WY, Tian Wang Y, **Rouleau GA**. Mutation of GABRA1 in an autosomal dominant form of juvenile myoclonic epilepsy. Nature Genetics 2002; 31:184-9

237.Joober R, Boksa P, Benkelfat C, **Rouleau GA**. Genetics of Schizophrenia: From Animal Models to Clinical Studies. J Psych Neurosc 2002; 27:336-47

238.Howard HC, Dubé, M-P, Prévost C, Bouchard J-P, Mathieu J, **Rouleau GA**. Fine Mapping the Candidate Region for Peripheral Neuropathy With or Without Agenesis of the Corpus Callosum in the French Canadian Population. Eur J Hum Gen 2002; 10:406-12

239.Joober R, Gauthier J, Lal S, Bloom D, Lalonde P, **Rouleau GA**, Benkelfat C, Labelle A. Catechol-o-methyltransferase val-108/158-met gene variants associated with performance on the wisconsin card sorting test. Arch Gen Psychiatry. 2002; 59:662-3.

240.Desautels A, Turecki G, Montplaisir J, Brisebois K, Sequeira A, Adam B, **Rouleau GA**. Evidence for a genetic association between monoamine oxidase A and restless legs syndrome. Neurology 2002; 59(2):215-9.

241. Howard HC, Mount DB, Rochefort D, Byun N, Dupre N, Lu J, Fan X, Song L, Riviere JB, Prevost C, Horst J, Simonati A, Lemcke B, Welch R, England R, Zhan FQ, Mercado A, Siesser WB, George AL, McDonald MP, Bouchard JP, Mathieu J, Delpire E, **Rouleau GA**. The K-Cl cotransporter KCC3 is mutant in a severe peripheral neuropathy associated with agenesis of the corpus callosum. Nature Genetics 2002; 32: 384-92.

242. Zhao Y, Kumar RA, Baser ME, Evans DG, Wallace A, Kluwe L, Mautner VF, Parry DM, **Rouleau GA**, Joe H, Friedman JM. Intrafamilial Correlation of Clinical Manifestations in Neurofibromatosis 2 (NF2). Genet Epidemiol 2002; 23: 245-59.

243. Dobson-Stone C, Danek A, Rampoldi L, Hardie RJ, Chalmers RM, Wood NW, Bohlega S, Dotti MT, Federico A, Shizuka M, Tanaka M, Watanabe M, Ikeda Y, Brin M, Goldfarb LG, Karp BI, Mohiddin S, Fananapazir L, Storch A, Fryer AE, Maddison P, Sibon I, Trevisol-Bittencourt PC, Singer C Caballero IR, Aasly JO, Schmierer K, Dengler R, Hiersemenzel LP, Zeviani M, Meiner V, Lossos A, Johnson S, Mercado FC, Sorrentino G, Dupre N, **RouleauGA**, Volkmann J, Arpa J, Lees A, Geraud G, Chouinard S, Nemeth A, Monaco AP. Mutational spectrum of the CHAC gene in patients with chorea-acanthocytosis. Eur J Hum Genet 2002; 10: 773-81.

244. Joober R, Zarate JM, **Rouleau GA**, Skamene E, Boksa P. Provisional mapping of quantitative trait loci modulating the acoustic startle response and prepulse inhibition of acoustic startle. Neuropsychopharmacology 2002; 27:765-81.

245. Desautels A, Michaud M, Montplaisir J, Turecki G, **Rouleau GA**. Restless leg syndrome arousal: clinic, etiology and genetic perspectives. Rev Neurol (Paris). 2002; 158:1225-31.

246. Gros-Louis F, Meijer IA, Hand CK, Dube MP, MacGregor DL, Seni MH, Devon RS, Hayden MR, Andermann F, Andermann E, **Rouleau GA**. An ALS2 gene mutation causes hereditary spastic paraplegia in a Pakistani kindred. Ann Neurol 2003; 53:144-5.

247. Yamamoto K, Cubells JF, Gelernter J, Benkelfat C, Lalonde P, Bloom D, Lal S, Labelle A, Turecki G, **Rouleau GA**, Joober R. Dopamine Beta-Hydroxylase (DBH) gene and schizophrenia phenotypic variability: A genetic association study. Am J Med Genet 2003 117B:33-8.

248. Cossette P, Loukas A, Lafreniere RG, Rochefort D, Harvey-Girard E, Ragsdale DS, Dunn RJ, **Rouleau GA**. Functional characterization of the D188V mutation in neuronal voltage-gated sodium channel causing generalized epilepsy with febrile seizures plus (GEFS). Epilepsy Res 2003; 53:107-17.

249. Gauthier J, Joober R, Mottron L, Laurent S, Fuchs M, De Kimpe V, **Rouleau GA**. Mutation screening of FOXP2 in individuals diagnosed with autistic disorder. Am J Med Genet 2003 118(2):172-5.

250. Turecki G, Sequeira A, Gingras Y, Seguin M, Lesage A, Tousignant M, Chawky N, Vanier C, Lipp O, Benkelfat C, **Rouleau GA**. Suicide and serotonin: Study of variation at seven serotonin receptor genes in suicide completers. Am J Med Genet 2003, 118B(1):36-40

251. Fan X, **Rouleau GA**. Progress in understanding the pathogenesis of oculopharyngeal muscular dystrophy. Can J Neurol Sci 2003, 30:8-14.

252. Szijan I, Rochefort D, Bruder C, Surace E, Machiavelli G, Dalamon V, Cotignola J, Ferreiro V, Campero A, Basso A, Dumanski JP, **Rouleau GA**. NF2 tumor suppressor gene: a comprehensive and efficient detection of somatic mutations by denaturing HPLC and microarray-CGH. Neuromolecular Med 2003;3(1):41-52.

253.Sequeira A, Kim C, Seguin M, Lesage A, Chawky N, Desautels A, Tousignant M, Vanier C, Lipp O, Benkelfat C, **Rouleau GA**, Turecki G. Wolfram syndrome and suicide: Evidence for a role of WFS1 in suicidal and impulsive behavior. Am J Med Genet 2003 ;119B(1):108-13.

254.Dupre N, Verlaan DJ, Hand CK, Laurent SB, Turecki G, Davenport WJ, Acciarri N, Dichgans J, Ohkuma A, Siegel AM, **Rouleau GA**. Linkage to the CCM2 locus and genetic heterogeneity in familial cerebral cavernous malformation. Can J Neurol Sci 2003 30(2):122-8.

255.El-Maarri O, Seoud M, Coullin P, Herbiniaux U, Oldenburg J, **Rouleau GA**, Slim R. Maternal Alleles acquiring paternal methylation patterns in biparental complete hydatidiform moles. Hum Mol Genet 2003 12(12):1405-1413.

256.Toulouse A, Rochefort D, Roussel J, Joober R, **Rouleau GA**. Molecular cloning and characterization of human RAI1, a gene associated with schizophrenia. Genomics 2003 8(2):162-71.

257.Segurado R, Detera-Wadleigh SD, Levinson DF, Lewis CM, Gill M, Numberger JI Jr, Craddock N, DePaulo JR, Baron M, Gershon ES, Ekholm J, Cichon S, Turecki G, Claes S, Kelsoe JR, Schofield PR, Badenhop RF, Morissette J, Coon H, Blackwood D, McInnes LA, Foroud T, Edenberg HJ, Reich T, Rice JP, Goate A, McInnis MG, McMahon FJ, Badner JA, Goldin LR, Bennett P, Willour VL, Zandi PP, Liu J, Gilliam C, Juo SH, Berrettini WH, Yoshikawa T, Peltonen L, Lonnqvist J, Nothen MM, Schumacher J, Windemuth C, Rietschel M, Propping P, Maier W, Alda M, Grof P, **Rouleau GA**, Del-Favero J, Van Broeckhoven C, Mendlewicz J, Adolfsson R, Spence MA, Luebbert H, Adams LJ, Donald JA, Mitchell PB, Barden N, Shink E, Byerley W, Muir W, Visscher PM, Macgregor S, Gurling H, Kalsi G, McQuillin A, Escamilla MA, Reus VI, Leon P, Freimer NB, Ewald H, Kruse TA, Mors O, Radhakrishna U, Blouin JL, Antonarakis SE, Akarsu N. Genome Scan Meta-Analysis of Schizophrenia and Bipolar Disorder, Part III: Bipolar Disorder. Am J Hum Genet 2003; 73(1):49-62.

258.Dupre N, Howard HC, Mathieu J, Karpati G, Vanasse M, Bouchard JP, Carpenter S, **Rouleau GA**. Hereditary motor and sensory neuropathy with agenesis of the corpus callosum. Ann Neurol 2003 54(1):9-18.

259.Laurans MS, DiLuna ML, Shin D, Niazi F, Voorhees JR, Nelson-Williams C, Johnson EW, Siegel AM, Steinberg GK, Berg MJ, Scott RM, Tedeschi G, Enevoldson TP, Anson J, **Rouleau GA**, Ogilvy C, Awad IA, Lifton RP, Gunel M. Mutational analysis of 206 families with cavernous malformations. J Neurosurg 2003 99(1):38-43.

260.Howard HC, Dupre N, Mathieu J, Bouchard JP, **Rouleau GA**. Severe neuropathy with agenesis of the corpus callosum. Médecine Sciences 2003 19(4):414-6.

261.Devon R, Helm J, **Rouleau G**, Leitner Y, Lerman-Sagie T, Lev D, Hayden M. The first nonsense mutation in alsin results in a homogeneous phenotype of infantile-onset ascending spastic paralysis with bulbar involvement in two siblings. Clin Genet 2003 64(3):210-215.

262.Chan EM, Bulman DE, Paterson AD, Turnbull J, Andermann E, Andermann F, **Rouleau GA**, Delgado-Escueta AV, Scherer SW, Minassian BA. Genetic mapping of a new Lafora progressive myoclonus epilepsy locus (EPM2B) on 6p22. J Med Genet 2003; 40:671-5.

263.Chan EM, Young EJ, Ianzano L, Munteanu I, Zhao X, Christopoulos CC, Avanzini G, Elia M, Ackerley CA, Jovic NJ, Bohlega S, Andermann E, **Rouleau GA**, Delgado-Escueta AV, Minassian BA, Scherer SW. Mutations in NHLRC1 cause progressive myoclonus epilepsy. Nature Genetics 2003; 35(2):125-7.

264.Abu-Baker A, Messaed C, Laganiere J, Gaspar C, Brais B, **Rouleau GA**. Involvement of the ubiquitin-proteasome pathway and molecular chaperones in oculopharyngeal muscular dystrophy (OPMD). Hum Mol Genet 2003;12(20):2609-23.

265.Fan X, Messaed C, Dion P, Laganiere J, Brais B, Karpati G, **Rouleau GA**. HnRNP A1 and A/B interaction with PABPN1 in oculopharyngeal muscular dystrophy. Can J Neurol Sci 2003; 30(3):244-51.

266.Koenekoop RK, Loyer M, Hand CK, Al Mahdi H, Dembinska O, Beneish R, Racine J, **Rouleau GA**. Novel RPGR mutations with distinct retinitis pigmentosa phenotypes in French-Canadian families. Am J Ophthalmol 2003; 136(4):678-87.

267.Lavoie H, Debeane F, Trinh QD, Turcotte JF, Corbeil-Girard LP, Dicaire MJ, Saint-Denis A, Page M, **Rouleau GA**, Brais B. Polymorphism, shared functions and convergent evolution of genes with sequences coding for polyalanine domains. Hum Mol Genet 2003; 12(22):2967-79

268.Liquori CL, Berg MJ, Siegel AM, Huang E, Zawistowski JS, Stoffer T, Verlaan D, Balogun F, Hughes L, Leedom TP, Plummer NW, Cannella M, Maglione V, Squitieri F, Johnson EW, **Rouleau GA**, Ptacek L, Marchuk DA. Mutations in a Gene Encoding a Novel Protein Containing a Phosphotyrosine-Binding Domain Cause Type 2 Cerebral Cavernous Malformations. Am J Hum Genet 2003; 73:1459-1464

269.Gros-Louis F, Laurent S, Lopes AA, Khoris J, Meininger V, Camu W, **Rouleau GA**. Absence of mutations in the hypoxia response element of VEGF in ALS. Muscle Nerve 2003 28(6):774-775

270.Hand CK, Devon RS, Gros-Louis F, Rochefort D, Khoris J, Meininger V, Bouchard JP, Camu W, Hayden MR, **Rouleau GA**. Mutation Screening of the ALS2 Gene in Sporadic and Familial Amyotrophic Lateral Sclerosis. Arch Neurol 2003; 60(12):1768-71

271.Forget-Dubois N, Pérusse D, Turecki G, Girard A, Billette J-M, **Rouleau GA**, Boivin M, Malo J, Tremblay RE. Diagnosing zygosity in infant twins: physical similarity, genotyping, and chorionicity. Twin Research 2003;6(6): 479-485.

272.Desautels A, Turecki G, Montplaisir J, Brisebois K, Desautels AK, Adam B, **Rouleau GA**. Analysis of CAG Repeat Expansions in Restless Legs Syndrome. Sleep 2003; 26(8):1055-7.

273.Sun X, Young LT, Wang JF, Grof P, Turecki G, **Rouleau GA**, Alda M. Identification of Lithium-Regulated Genes in Cultured Lymphoblasts of Lithium Responsive Subjects with Bipolar Disorder. Neuropsychopharmacology 2004; 29 : 799-804

274.Desautels A, Turecki G, Xiong L, Rochefort D, Montplaisir J, **Rouleau GA**. Mutational Analysis of Neurotensin in Familial Restless Legs Syndrome. Mov Disord 2004; 19(1): 90-4.

275.Jafari-Schluep HF, Khoris J, Mayeux-Portas V, Hand C, **Rouleau G**, Camu W; Et le Groupe Francais d'etude des Maladies du Motoneurone. Superoxyde dismutase 1 gene abnormalities in familial amyotrophic lateral sclerosis: phenotype/genotype correlations: The French experience and review of the literature Rev Neurol. 2004 160(1):44-50.

276.Lafreniere RG, MacDonald ML, Dube MP, MacFarlane J, O'Driscoll M, Brais B, Meilleur S, Brinkman RR, Dadivas O, Pape T, Platon C, Radomski C, Risler J, Thompson J, Guerra-Escobio AM, Davar G, Breakefield XO, Pimstone SN,

Green R, Pryse-Phillips W, Goldberg YP, Younghusband HB, Hayden MR, Shemington R, **Rouleau GA**, Samuels ME. Identification of a Novel Gene (HSN2) Causing Hereditary Sensory and Autonomic Neuropathy Type II through the Study of Canadian Genetic Isolates. Am J Hum Genet. 2004 74(5):1064-73

277.Verlaan DJ, Laurent SB, Sure U, Bertalanffy H, Andermann E, Andermann F, **Rouleau GA**, Siegel AM. CCM1 mutation screen of sporadic cases with cerebral cavernous malformations. Neurology 2004 62(7):1213-5.

278.Diaz-Anzaldua A, Joober R, Riviere JB, Dion Y, Lesperance P, Richer F, Chouinard S, **Rouleau GA**. Tourette syndrome and dopaminergic genes: a family-based association study in the French Canadian founder population. Mol Psychiatry. 2004 9(3):272-7.

279.Diaz-Anzaldua A, Joober R, Riviere JB, Dion Y, Lesperance P, Chouinard S, Richer F, **Rouleau GA**. Association between 7q31 markers and Tourette syndrome. Am J Med Genet. 2004 5;127A(1):17-20.

280.Verlaan DJ, Laurent S, Rochefort DL, Liquori CL, Marchuk, DA, Siegel AM, **Rouleau GA**. CCM2 mutations account for 13% of cases in a large collection of kindreds with hereditary cavernous malformations. Ann Neurol 2004 55(5):757-758

281.Levchenko A, Montplaisir JY, Dube MP, Riviere JB, St-Onge J, Turecki G, Xiong L, Thibodeau P, Desautels A, Verlaan DJ, **Rouleau GA**. The 14q restless legs syndrome locus in the French Canadian population. Ann Neurol 2004 55(6):887-91.

282.Valdmanis PN, Simoes Lopes AA, Gros-Louis F, Stewart JD, **Rouleau GA**, Dupré N. Autosomal dominant sensory ataxia: identification of a new neurodegenerative disorder with linkage to 8p12-8q12.1. J Med Genet 2004 41(8):634-9

283.Gros-Louis F, Lariviere R, Gowing G, Laurent S, Camu W, Bouchard JP, Meininger V, **Rouleau GA**, Julien JP. A frameshift deletion in peripherin gene associated with amyotrophic lateral sclerosis. J Biol Chem 2004 279(44):45951-6

284.Valdmanis PN, Simoes Lopes AA, Gros-Louis F, Stewart JD, **Rouleau GA**, Dupre N. A novel neurodegenerative disease characterised by posterior column ataxia and pyramidal tract involvement maps to chromosome 8p12-8q12.1. J Med Genet 2004 41(8):634-9.

285.Lesperance P, Djerroud N, Diaz Anzaldua A, **Rouleau GA**, Chouinard S, Richer F. Restless legs in Tourette syndrome. Mov Disord 2004 19(9):1084.

286.Levchenko A, Robitaille Y, Strong MJ, **Rouleau GA**. TAU mutations are not a predominant cause of frontotemporal dementia in Canadian patients. Can J Neurol Sci 2004 31(3):363-7.

287.Gauthier J, Bonnel A, St-Onge J, Karemera L, Laurent S, Mottron L, Fombonne E, Joober R, **Rouleau GA**. NLGN3/NLGN4 gene mutations are not responsible for autism in the Quebec population. Am J Med Genet 2004 Epub ahead of print

288.Riviere JB, Verlaan DJ, Shekarabi M, Lafreniere RG, Benard M, Der Kaloustian VM, Shbaklo Z, **Rouleau GA**. A mutation in the HSN2 gene causes sensory neuropathy type II in a Lebanese family. Ann Neurol 2004 55(4):572-5.

289.Meijer IA, Cossette P, Roussel J, Benard M, Toupin S, **Rouleau GA**. A novel locus for pure recessive hereditary spastic paraplegia maps to 10q22.1-10q24.1. Ann Neurol 2004 56(4):579-82.

290.Grewal KK, Stefanelli MG, Meijer IA, Hand CK, **Rouleau GA**, Ives EJ. A founder effect in three large Newfoundland families with a novel clinically variable spastic ataxia and supranuclear gaze palsy. Am J Med Genet. 2004 131A(3):249-54.

291.Verlaan DJ, Laurent SB, **Rouleau GA**, Siegel AM. No CCM2 mutations in a cohort of 31 sporadic cases. Neurology 2004 63(10):1979.

292.Cossette P, Lortie A, Vanasse M, Saint-Hilaire JM, **Rouleau GA**. Autosomal dominant juvenile myoclonic epilepsy and GABRA1. Adv Neurol. 2005 95:255-63

293.Xiong L, **Rouleau GA**, Delisi LE, St-Onge J, Najafee R, Riviere JB, Benkelfat C, Tabbane K, Fathalli F, Danics Z, Labelle A, Lal S, Joober R. CAA insertion polymorphism in the 3'UTR of Nogo gene on 2p14 is not associated with schizophrenia. Brain Res Mol Brain Res 2005 133(1):153-6.

294.Devon RS, Schwab C, Topp JD, Orban PC, Yang YZ, Pape TD, Helm JR, Davidson TL, Rogers DA, Gros-Louis F, **Rouleau G**, Horazdovsky BF, Leavitt BR, Hayden MR. Cross-species characterization of the ALS2 gene and analysis of its pattern of expression in development and adulthood. Neurobiol Dis 2005 18(2):243-57.

295.Siegel AM, Bertalanffy H, Dichgans JJ, Elger CE, Hopf H, Hopf N, Keidel M, Kleider A, Nowak G, Pfeiffer RA, Schramm J, Spuck S, Stefan H, Sure U, Baumann CR, **Rouleau GA**, Verlaan DJ, Andermann E, Andermann F. [Familial cavernous malformations of the central nervous systemA clinical and genetic study of 15 German families]. Nervenarzt. 2005 76(2):175-80.

296.Dion P, Shanmugam V, Gaspar C, Messaed C, Meijer I, Toulouse A, Laganiere J, Roussel J, Rochefort D, Laganiere S, AllenC, Karpati G, Bouchard JP, Brais B and **Rouleau GA**. Transgenic expression of an expanded $(GCG)_9$ repeat PABPN1 leads to weakness and coordination defects in mice. Neurobiology of Disease 2005 18(3):528-536.

297.Corbeil-Girard LP, Klein AF, Sasseville AM, Lavoie H, Dicaire MJ, Saint-Denis A, Page M, Duranceau A, Codere F, Bouchard JP, Karpati G, **Rouleau GA**, Massie B, Langelier Y, Brais B. PABPN1 overexpression leads to upregulation of genes encoding nuclear proteins that are sequestered in oculopharyngeal muscular dystrophy nuclear inclusions. Neurobiol Dis 2005 18(3): 351-67

298.El-Maarri O, Seoud M, Riviere JB, Oldenburg J, Walter J, **Rouleau G**, Slim R. Patients with familial biparental hydatidiform moles have normal methylation at imprinted genes. Eur J Hum Genet 2005 13(4):486-90.

299.Roddier K, Thomas T, Marleau G, Gagnon AM, Dicaire MJ, St-Denis A, Gosselin I, Sarrazin AM, Larbrisseau A, Lambert M, Vanasse M, Gaudet D, **Rouleau GA**, Brais B. Two mutations in the HSAN2 in French Canadians. Neurology 2005;64:1762-1767

300.Desautels A, Turecki G, Montplaisir J, Xiong L, Walters AS, Ehrenberg BL, Brisebois K, Desautels AK, Gingras Y, Johnson WG, Lugaresi E, Coccagna G, Picchietti DL, Lazzarini A, **Rouleau GA**. Restless Legs Syndrome : confirmation of linkage to chromosome 12q, genetic heterogeneity and evidence of complexity. Arch Neurol 2005 62(4):591-6.

301.Baser ME, Kuramoto L, Woods R, Joe H, Friedman JM, Wallace AJ, Ramsden RT, Olschwang S, Bijlsma E, Kalamarides M, Papi L, Kato R, Carroll J, Lázaro C, Joncourt F, Parry DM, **Rouleau GA**, Evans GR. The location of constitutional neurofibromatosis 2 (NF2) splice-site mutations is associated with the severity of NF2. J Med Genet 2005;42:40-6

302.Alda M, Grof P, **Rouleau GA**, Turecki G, Young LT. Investigating responders to lithium prophylaxis as a strategy for mapping susceptibility genes for bipolar disorder. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:1038-45

303.Krampfl K, Maljevic S, Cossette P, Ziegler E, **Rouleau GA**, Lerche H, Bufler J. Molecular analysis of the A322D mutation in the GABA$_A$ receptor α_1-subunit causing juvenile myoclonic epilepsy. Eur J Neurosci 2005;22:10-20

304.Joober R, **Rouleau GA,** Lal S, Bloom D, Lalonde P, Labelle A, Benkelfat C. Increased prevalence of schizophrenia spectrum disorders in relatives of neuroleptic-nonresponsive schizophrenic patients. Schizophr Res 2005 ;77:35-41

305.Nikpoor Borzoo, Duan QL, **Rouleau GA**. Acute adverse reactions associated with angiotensin-converting enzyme inhibitors: genetic factors and therapeutic implications. Expert Opin Pharmacother 2005;6:1851-6

306.Meyer J, Johannssen K, Freitag CM, Schraut K, Teuber I, Hahner A, Mainhardt C, Mössner R, Volz HP, Wienker TF, McKeane D, Stephan DA, **Rouleau GA**, Reif A, Lesch KP. Rare variants of the gene encoding the potassium-chloride cotransporter 3 are associated with bipolar disorder. Int J Neuropsychopharmacol 2005;8:495-504

307.Gauthier J, de Amorim G, Mnatzakanian GN, Saunders C, Vincent JB, Toupin S, Lacasse H, Kauffman D, St-Onge J, Laurent S, Macleod PM, Minassian BA, **Rouleau GA**. Clinical Stringency Greatly Improves Mutation Detection in Rett Syndrome. Can J Neurol Sci 2005;32:321-6

308.Abu-Baker A, Laganiere S, Fan X, Laganiere J, Brais B and **Rouleau GA**. Cytoplasmic targeting of mutant poly (a)-binding protein nuclear 1 suppresses protein aggregation and toxicity in oculopharyngeal muscular dystrophy. Traffic 2005;6:766-79.

309.Rusbridge C, Knowler P, **Rouleau GA**, Minassian BA and Rothuizen J. Inherited Occipital Hypoplasia/Syringomyelia in the Cavalier King Charles Spaniel : Experiences in Setting Up a world wide DNA Collection. J Hered 2005;96:745-9

310.Diaz-Anzaldua A, Rivière JB, Dubé MP, Joober R, Saint-Onge J, Dion Y, Lespérance P, Richer F, Chouinard S, **Rouleau GA** and the Montreal Tourette Syndrome Study Group. Chromosome 11-q24 region in Tourette Syndrome : Association and linkage disequilibrium study in the French Canadian population. Am J Med Genet 2005;38:225-8.

311.Toulouse A, Au-Yeung F, Gaspar C, Roussel J, Dion P and **Rouleau GA**. Ribosomal frameshifting on MJD transcripts with long CAG tracts. Hum Mol Genet 2005;14:2649-60.

312.Duan QL, Nikpoor B, Dubé MP, Molinaro G, Meyer IA, Dion P, Rochefort D, Saint-Onge J, Flury L, Brown NJ, Gainer JV, Rouleau JL, Agostoni A, Cugno M, Simon P, Clavel P, Potier J, Wehbe B, Benarbia S, Marc-Aurèle J, Chanard J, Foroud T, Adam A, **Rouleau GA**. A variant in XPNPEP2 is associated with angiodema induced by angiotensin-converting enzime inhibitors. Am J Hum Genet 2005 ;77:617-26.

313.Millecamps S, Gentiol BJ, Gros-Louis F, **Rouleau GA**, Julien JP. Alsin is partially associated with centrosome in

human cells. Biochim Biophys Acta 2005;1745:84-100.

314.Buckley PG, Mantripragada KK, Diaz de Stahl T, Piotrowski A, Hansson CM, Kiss H, Vetrie D, Ernberg IT, Nordenskjold M, Bolund L, Sainio M, **Rouleau GA**, Niimura M, Wallace AJ, Evans DG, Grigelionis G, Menzel U, Dumanski JP. Identification of genetic aberrations on chromosome 22 outside the NF2 locus in schwannomatosis and neurofibromatosis type 2. Hum Mutat 2005;26:540-9

315.Dumais A, Lesage AD, Alda M, **Rouleau GA,** Dumont M, Chawky N, Roy M, Mann JJ, Benkelfat C, Turecki G. Risk factors for suicide completion in major depression: a case-control study of impulsive and aggressive behaviors in men. Am J Psychiatry 2005;162:2116-24

316.Verlaan DJ, Roussel J, Laurent SB, Elger CE, Siegel AM, **Rouleau GA**. CCM3 mutations are uncommon in cerebral cavernous malformations. Neurology 2005;65 :1982-3

317.Sequeira A, Gwadry FG, Ffrench-Mullen JM, Canetti L, Gingras Y, Casero RA Jr, **Rouleau GA**, Benkelfat C, Turecki G. Implication of SSAT by Gene Expression and Genetic Variation in Suicide and Major Depression. Arch Gen Psychiatry 2006;63:35-48

318.de Lara CL, Dumais A, **Rouleau G**, Lesage A, Dumont M, Chawki N, Alda M, Benkelfat C, Turecki G. Stin2 Variant and Family History of Suicide as Significant Predictors of Suicide Completion in Major Depression. Biol Psychiatry 2006;59:114-20.

319.Gauthier J, Joober R, Dubé MP, Verlaan DJ, St-Onge J, Bonnel A, Garépy D, Lacasse H, Najafee R, Fombonne E, Mottron L, **Rouleau GA**. Autism Spectrum Disorders Associated with X Chromosome Markers in French-Canadian Males. Mol Psychiatry 2006;11:206-13.

320.Murdoch S, Djuric U, Mazhar B, Seoud M, Khan R, Kuick R, Bagga R, Kircheisen R, Ao A, Ratti B, Hanash S, **Rouleau GA**, Slim R. Mutations in NALP7 cause recurrent hydatidiform moles and reproductive watage in humans. Nat Genet 2006;38:300-2.

321.Brinkman RR, Dubé MP, **Rouleau GA,** Orr A, Samuels ME. Human monogenic disorders – a source of novel drug targets. Nat Rev Genet 2006;7:249-60.

322.McCaffery JM, Frasure-Smith N, Dubé MP, Théroux P, **Rouleau GA**, Duan Q and Lespérance F. Common genetic vulnerability to depressive symptoms and coronary artery disease : a review and development of candidate genes related to inflammation and serotonin. Psychosom Med 2006;68:187-200.

323.Verlaan DJ, Dubé MP,St-Onge J, Noreau A, Roussel J, Satgé N, Wallace C, **Rouleau GA.** A new locus for autosomal dominant intracranial aneurysm, ANIB4, maps to chromosome 5p15.2-14.3. J Med Genet 2006;43:e31.

324.Thiffault I, Rioux MF, Tetreault M, Jarry J, Loiselle L, Poirier J, Gros -Louis F, Mathieu J, Vanasse M, **Rouleau GA**, Bouchard JP, Lesage J, Brais B. A new autosomal recessive spastic ataxia associated with frequent white matter changes maps to 2q33-34. Brain 2006;129:2332-40

325.Sasseville MJ, Caron AW, Bourget L, Klein AF, Ficaire MJ, **Rouleau GA**, Massie B, Langelier Y, Brais B. The dynamism of PABPN1 nuclear inclusions during the cell cycle. Neurobiol Dis 2006;23:621-9

326.Sengupta S, Xiong L, Fathalli F, Benkelfat C, Tabbane K, Danics Z, Labelle A, Lal S, Krebs MO, **Rouleau GA**, Joober

R. Association study of the trinucleotide repeat polymorphism within SMARCA2 and schizophrenia. BMC Genet 2006;3:7-34

327. Dupre N, Bouchard JP, Brais B, **Rouleau GA**. Hereditary ataxia, spastic paraparesis and neuropathy in the French-Canadian population. Can J Neurol Sci 2006;33:149-57.

328. Torkamanzehi A, Boksa P, Ayoubi M, Fortier ME, Ng Ying Kin NM, Skamene E, **Rouleau G**, Joober R. Identification of informative strains and provisional QTL mapping of amphetamine (AMPH)-induced locomotion in recombinant congenic strains (RCS) of mice. Behav Genet 2006;36:903-13.

329. Molinaro G, Duan QL, Chagnon M, Moreau ME, Simon P, Clavel P, Lavaud S, Boileau G, **Rouleau GA**, Lepage Y, Adam A, Chanard J. Kinin-dependent hypersensitivty reactions in hemodialysis : Metabolic and genetic factors. Kidney International 2006;70:1823-31.

330. Levchenko A, Provost S, Montplaisir JY, Xiong L, St-Onge J, Thibodeau P, Rivière JB, Desautels A, Turecki G, Dubé MP, **Rouleau GA**. A novel autosomal dominant restless legs syndrome locus maps to chromosome 20p13. Neurology 2006;67:900-1.

331. Jindal HK, Yoshinaga K, Seo PS, Lutchman M, Dion PA, **Rouleau GA**, Hanada T, Chishti AH. Purification of the NF2 tumor suppressor protein from human erythrocytes. Can J Neurol Sci 2006 In press

332. Gros-Louis F, Gaspar C and **Rouleau GA**. Genetics of familial and sporadic amyotrophic lateral sclerosis. Biochim Biophys Acta 2006 In press

333. Kharma N, Moghnieh H, Yao J, Guo YP, Abu-Baker A, Laganiere J, **Rouleau G** and Cheriet M. Automatic Segmentation of Cells from Microscopic Imagery using Ellipse Detection. IEE Proc. Vision & image signal Processing 2006 in press.

334. Valdmanis P, Brunet D, St-Onge J, Weston L, **Rouleau GA**, Dupre N. A founder haplotype for autosomal dominant sensory ataxia in Eastern Canada. Neurology 2006 in press

335. Knirions P, **Rouleau GA**. Administration of testosterone results in reversible deterioration in Kennedy's disease. J Neurol Neurosurg Psychiatry 2006 in press

336. Abu-Baker A, **Rouleau GA.** Oculopharyngeal muscular dystrophy : Recent advances in the understanding of the molecular pathogenic mechanisms and treatment strategies. Biochimica Biophysica Acta 2006 in press

337. The Tourette Syndrome Association International Consortium for Genetics and the Centre national de génotypage. Genome scan for Tourette's disorder in affected sib-pair and multigenerational families. Am J Hum Genet 2006 in press

338. Gros-Louis F, Dupré N, Dion P, Fox MA, Laurent S, Verreault S, Sanes JR, Bouchard JP and Rouleau **GA**. Mutations in SYNE1 lead to a novel form of autosomal recessive cerebellar ataxia. Nat Genet 2006 in press

339. Jindal K, Yoshinaga K, Seo PS, Dion P, **Rouleau GA**, Hanada T and Chishti AH. Identification and purification of NF2 tumor suppressor protein from human erythrocytes. Can J Neurol Sci 2006 in press

340. Valdmanis P, Meijer IA, Reynolds A, Lei A, MacLeod P, Schlesinger D, Zatz M, Reid E, Dion P, Drapeau P and

Rouleau GA. Mutations in the *KIAA0196* gene at the *SPG8* locus cause Hereditary Spastic Paraplegia. Am J Hum Genet 2006 in press

Review Articles and Book Chapters

1. Seizinger B, Martuza R, **Rouleau G**, Breakefield XO and Gusella JF. Models for Inherited Susceptibility to Cancer in the Nervous System: A Molecular Genetic Approach to Neurofibromatosis. Developmental Neuroscience 1987; 9:144-153.

2. Martuza R, Seizinger B, Jacoby L, **Rouleau G** and Gusella JF: The Molecular Biology of Human Glial Tumours. Trends in Neuroscience 1988; 11:22-27.

3. Rouleau GA, Brown RH, Sheperd G, Trofatter JA, Conneally PM, Gusella JF. Linkage Studies in a Large Kindred with a Hereditary Sensory Neuropathy. In "Charcot-Marie Tooth Disorders" 1988, Alan R Liss, NY, 53:299-306.

4. Martuza R and **Rouleau G**. Genetic Aspects of Neurosurgical Problems. In Neurological Surgery edited by Youman. W.B. Saunders Co., Philadelphia 1989.

5. Brown RH, Horovitz HR, **Rouleau GA**, McKenna Yasick D, Beard C, Saap P, Haines J, Gusella JF, Figlewicz DA. Investigation of Gene Linkage in Familial Amyotrophic Lateral Sclerosis. Prepared for MDA International Conference of ALS and Other Motor Neuron Diseases. Tuscon 1989.

6. Kolodny EH, Boustany RM, **Rouleau GA**, Growden JH, Martin JB. Familial Spastic Paraplegia: Clinical Observations and Genetic Studies. Prog Clin Biol Res 1989; 306:206-11.

7. **Rouleau GA**, Gusella JF. Chromosome 22 and the Genesis of Meningioma and Acoustic Nneuroma. In Molecular Genetics in Cancer Diagnosis 1990, Jeffrey Cossman. Elsevier Science Publishing Co., NY, 409-419.

8. Figlewicz DA, Gusella JF, **Rouleau GA**. Gene Linkage Studies in Hereditary Amyotrophic Lateral Sclerosis. In Handbook of Amyotrophic Lateral Sclerosis edited by R. Smith, M.D. 1990.

9. Fontaine B, **Rouleau GA**, Seizinger BS, Menon AG, Jewell AF, Martuza RL, Gusella JF. Molecular Genetics of Neurofibromatosis 2 and Related Tumors (Acoustic Neuroma and Meningioma). Ann N.Y. Acad Sci 1991;615:338-43.

10. Brown RH, Horvitz R, **Rouleau GA**, McKenna-Yasek D, Beard C, Sapp P, Haines JL, Gusella JF, Figlewicz D. Gene Linkage in Familial Amyotrophic Lateral Sclerosis: A Progress Report. Adv Neurol 1991; 56: 215-226.

11. **Rouleau GA**, Gusella JF. Genetic Analysis of the Neurofibromatosis 2 Locus on Human Chromosome 22. In Molecular Genetic Approaches to Neuropsychiatric Diseases edited by Jurgen Brosius and Robert T. Fremeau. Academic Press Inc. San Diego, 1991; 203-214.

12. Figlewicz DA, **Rouleau GA.** Familial Motor Neurone Disease. In: Motor Neurone Disease. edited by Adrian C. Williams. 1993

13. **Rouleau GA**. Des Mutations du Gène de la Superoxide Dismutase Associées à la Maladie de Lou Gehrig. Médecine/Sciences 1993; 9:643.

14. **Rouleau GA**. Molecular Genetic Studies of Neurofibromatosis type 2. In The Neurofibromatoses: a pathogenetic and clinical overview . edited by Prof. RAC Hughes and Dr. SM Huson. Chapman and Hall Medical 1994; 50 -61.

15. Claudio J, Belliveau M, **Rouleau GA**. Neurofibromatosis Type 2. In: Meyers, R.A., ed. Encyclopedia of Molecular Biology and Molecular Medicine. VCH Verlagsgesellschaft. Weinheim. John Wiley & Sons, 1997.

16. Claudio J, **Rouleau GA**. Neurofibromatosis: type 1 and type 2. In: Textbook of Molecular Medicine. edited by J. Larry Jameson. 1376 pages. 1997

17. Ruttledge M, **Rouleau GA**. The Neurofibromatoses and Other Neuro-oncological Syndromes. In Inherited Susceptibility to Cancer. edited by William Foulkes and Shirley V. Hodgson. University Press. 1998; 264-278.

18. Dubé M.-P., **Rouleau GA**. Hereditary spastic paraplegia. In: Neurogenetics, contemporary neurology series, 57. Edited by S.M. Pulst. Oxford University Press, 2000.

19. Claudio J, **Rouleau GA**. Neurofibromatosis type 2: Some Answers, More Questions. In: Encyclopedia of Neuroscience. edited by G. Adelman and B. Smith. Elsevier Science, 2001.

20. Brais B, **Rouleau GA**. Oculopharyngeal Muscular Dystrophy. In: GeneClinics: Clinical Genetic Information Resource [database online]. Copyright, University of Washington, Seattle. Available at http://www.geneclinics.org. March 2001.

21. Desautels A, Michaud M, Montplaisir J, Turecki G, **Rouleau G** Les impatiences musculaires de l'éveil. In: Neuropathies périphériques: polyneuropathies et mononeuropathies multiples. Bouche P. and Valate JM editors. Paris, 2001.

22. Desautels A, Michaud M, Montplaisir J, Turecki G, **Rouleau GA**. Le Syndrome d'impatiences musculaires de l'éveil: aspects cliniques, éléments d'étiologie et perspectives génétiques. Rev Neurol 2001.

23. Brais B, **Rouleau GA**. Oculopharyngeal Muscular Dystrophy. In: Neuromusculars Disorders in Clinical Practice. Edited by B. Katirji, HJ Kaminski, DC Preston, RL Ruff, and BE Shapiro. Butterworth Heinemann, 2002.

24. Marineau C et **Rouleau GA**. Pour une meilleure synergie entre les disciplines. Dans: Prisme: Défis et promesses en recherche clinique infantile **42**:153-157 (2003).

25. **Rouleau GA**, Rioux M-F. La neurofibromatose. Le spécialiste 2004; 6(1):12-13.

26. Xiong L, Gaspar C, **Rouleau GA**. Genetics of Alzheimer's Disease and Research Frontiers in Dementia (review). Geriatrics & Aging. 2005, 8(4):31-35.

27. Dupré N., Pradat P.F., Bouchard J.P., **Rouleau G.A.,** Meininger V. La sclérose latérale amyotrophique : une maladie d'origine génétique et environnementale. La Lettre du Neurologue 2005;9 :139-142

28. Tumbull J, Lohi H, Kearney JA, **Rouleau GA,** Delgado-Escueta AV, Meisler MH, Cossette P, Minassian BA. Sacred Disease Secrets Revealed : Hum Molec Genet 2005;14:2491-2500

29. Cossette P. and **Rouleau GA**. Monogenic Epilepsies in Humans : Molecular Mechanisms and Relevance for the study of Intractable Epilepsy. Adv Neurol 2006;97:381-8

30. Ruttledge MH, **Rouleau GA**. Role of the neurofibromatosis Type 2 in the development of tumors of the nervous system. Neurosurg Focus 2005;19:E6

31. Abu-Baker A and Rouleau GA. Polyalanine and polyglutamine diseases: possible common mechanisms ? In: Genet Instabilities and Neurological Diseases. Edited by Robert D. Wells and Tetsuo Ashizawa. 2006;33:487-513.

32. **Rouleau GA.** Molecular Genetic Studies of Neurofibromatosis type 2. In Neurofibromatosis: von Recklinghhausen's Disease and Other Neurofibromatoses. edited by Prof. RAC Hughes and Dr. SM Huson. In press.

33. Xiong L., Turecki G., Levchenko A., Gaspar C., Montplaisir J., **Rouleau GA.** Genetics of Restless Legs Syndrome. In: Restless Legs Syndrome. Edited by Hening W., Allen R., Chokroverty S. et al. Butterworth-Heinemann Ltd. 2006, 384p.

Presentation (selected)

Guess speaker

1. *CAG and GCG trinucleotide repeats: do they have anything in common?* Département de pathologie et de biologie cellulaire de l'Université de Montréal, Montréal, Canada. August 1999.
2. *Genetics of Epilepsy.* Hôpital Sainte-Justine, Montréal, Canada. January 2001.
3. Residence Seminars on Movement Disorders, Bromont, Canada. February 8-11, 2001
4. *Genetics of Epilepsy and Molecular Biology of OPMD*. Ryad, Saudi Arabia. February 15-16, 2001.
5. *Genetics of Mental Disorders*. Université de Montréal, Montréal, Canada. March 16, 2001
6. *Genetics of Schizophrenia and Bipolar Disease.* Ixtapa, Mexico. April 20, 2001.
7. Association des médecins généticiens du Québec, Réunion scientifique et assemblée générale annuelle, Québec, Canada. May 2001
8. *La maladie neuromusculaire, l'éthique médicale et la sclérose latérale amyotrophique*. Association des neurologues du Québec. Québec, Canada. September 14-16, 2001.
9. *Génétique des maladies du motoneurone de l'adulte : nouvelles avancées*. Université de Montpellier. Montpellier, France. November 5, 2001.
10. *Impact clinique des neurosciences*. Université de Montréal. Montréal, Canada. January 16, 2002.
11. *Genetics of Epilepsies*. Dept. of Neurology and Neusciences, University of Calgary. Calgary, Canada. April 17-19, 2002
12. *Genetics of Epilepsies and Genetics of Amyotrophic Lateral sclerosis*. Middle East Medical Assembly. American University of Beirut. Beirut, Lebanon. May 1-5, 2002
13. *The Genetics of RLS: discovery of a genetic linkage to RLS*. Associated Professional Sleep Societies. Seattle, USA. June 10, 2002
14. State of the Art of Restless Legs Syndrome: Current Directions in the Search of its Cause, Cure and Treatment. Symposium, November 2002.
15. *Molecular Genetics of Oculopharyngeal Muscular Dystrophy, a PolyAlanine Disorder.* University of Pennsylvania. Philadelphia, USA. January 2003

16. *Molecular Mechanism of Hereditary Ataxias*. Neurobiology Review Course, Canadian Congress of Neurological Sciences. Québec, Canada. June 17-21, 2003.
17. *Écogénétique des réactions anaphylactoïdes en hémodialyse*. 5e réunion annuelle de la Société de Néphrologie et Société française de dialyse. Lyon, France. October 2, 2003
18. *La génétique du syndrome Gilles-de-la-Tourette*. Centre de recherche de l'Hôpital Sainte-Justine. Montréal, Canada. October 10, 2003
19. *Génétique en Psychiatrie: Étude du syndrome de Tourette*. Centre de recherche du CHUM, Hôpital Saint-Luc. Montréal, Canada. 2003
20. Univiersity of Alberta. Alberta, Canada. 10 et 11 décembre 2003
21. *Molecular Pathogenesis of OPMD*. New Directions in Biology and Disease of Skeletal Muscle. San Diego, USA. 25-27 janvier 2004
22. *Génétique du syndrome de Gilles de la Tourette*. Service de médecine génique, Centre hospitalier de l'Université de Montréal. Montréal, Canada. 13 février 2004
23. *Molecular Pathogenesis of OPMD*. Hôpital Ste-Justine. Montréal, Canada. 18 février 2004
24. 4th International Conference on Unstable Microsatellites and Human Diseases. Banff, Canada. 28 février – 4 mars 2004
25. Développement neurobiologique et comportement. Conférencier et modérateur d'une table ronde organisée dans le cadre de la retraite scientifique du CHU-Mère-Enfant. Hôpital Sainte-Justine. Montréal, Canada. 17 avril 2004.
26. *Les gènes et le cerveau*. Dans le cadre des *Portes ouvertes sur les neurosciences*, Université de Montréal. Montréal, Canada. 18 avril 2004.
27. 20th TSA International Genetics Consortium Workshop. Chicago, Illinois, USA. September 11-12, 2004
28. *Les tics : aspects cliniques et génétiques*. Dans le cadre du Symposium 2004 de l'Association Québécoise du Syndrome de La Tourette : *Le Syndrome de La Tourette … bien plus que des tics !* Hôpital Louis-H. Lafontaine, Montréal, Canada. 24 septembre 2004.
29. *Le plan de développement en neurosciences*. Département de médecine, Centre hospitalier de l'Université de Montréal. Montréal, Canada. 13 octobre 2004.
30. *La médication du futur*. Dans le cadre du colloque Pharmarketing: Politique du médicament et valorisation de l'innovation biopharmaceutique: Un atout pour le Québec. Université de Montréal, Montréal, Canada. 14 octobre 2004.
31. *Le partage des informations médicales avec les proches : de la théorie aux pratiques*. Dans le cadre des Belles Soirées de l'Université de Montréal, Montréal, Canada. 21 octobre 2004.
32. *Keynote speech – Neurogenetics: From simple to complex traits*. Dans le cadre du Premier Colloque de NeuroSciences Cliniques ULB – CHUM. Campus Erasme (ULB), Bruxelles, Belgique. 20 novembre 2004.
33. *Molecular Genetics of Oculopharyngeal Muscular Distrophy*. Department of Neurology Grand Rounds, University of Rochester Medical Center, New-York, USA. February 4, 2005.
34. *Overview of Genetics*. Autism Research Training Scool. Montreal, Canada. August 23,2005.
35. *Overview of Genetic Mutations causing Motor Neuron Disease*. Symposium Amyotrophic Lateral Sclerosis : Causes and Therapeutic Perspectives. Montreal, Canada. September 9, 2005.
36. *Intracranial Aneurysm Genes in the Canadian Population*. Familial Intracranial Aneurysm (FIA) Mid-Study, Hawaï, USA. September 18, 2005.
37. *Intracellular chloride homeostasis in nervous system function and dysfunction*. First International Meeting on

Physiology and Pathology of Chloride Transporters and Channels. Soria, Spain. September 21, 2005.

38. *Genetics of Pain.* Journées de la Douleur. Montréal, Canada. October 1, 2005.
39. *La génétique des maladies neuro-dégénératives.* Congrès de la Société Québécoise de Biologie Clinique. Drummondville, Canada. October 21,2005.
40. *Neurosciences et neurogénomique.* Assemblée annuelle du Département de médecine de l'Université de Montreal, Canada. October 28, 2006.
41. *Genomic Studies of Brain Diseases.* Japan-Canada Joint Workshop on Brain Sciences. Tokyo, Japan. January 18, 2006.
42. *Genomic approaches to brain diseases.* Hotchkiss Brain Institute & Faculty of Medicine. Calgary, Canada. January 24, 2006.
43. *Genomics and the Study of Brain Diseases.* Ottawa Health Research Institute, Distinguished Professor Seminar Series. Ottawa, Canada. March 1, 2006.
44. *Molecular Genetics of autism and Gilles de la Tourette syndrome.* 5th National Congress of the Mexican Federation of pro-mental health societies. Acapulco, Mexico. March 25, 2006.
45. *Polyalanine Diseases.* Canadian Genetic Diseases Network Annual Scientific Meeting. Saint-Sauveur, Canada. April 22, 2006.
46. *Genomic Approaches to Brain Diseases.* CHUL Reaerch Center. Quebec, Canada. May 26, 2006.
47. *Genomic Approaches to Brain Diseases.* Department of Pathology and Cellular Biology 23th Annual Scientific Meeting, Université de Montréal. Montreal, Canada. June 1, 2006
48. *Molecular Approaches to Identifying Genetic Causes of Movement Disorders.* Canadian Congress for Neurological Sciences. Montreal, Canada. June 14, 2006.
49. *Molecular Investigation of Oculopharyngeal Muscular Dystrophy.* International Congress on Neuromuscular Diseases. Istanbul, Turkey. July 4, 2006.
50. *Healthcare and Research in Genetics : Access and Use of Medical Data.* Symposium 2006, International Institute of Research inEthics and Biomedicine. Toulouse, France. August 9, 2006.
51. *Emerillon Therapeutics Inc.* Biocontact 2006. Québec, Canada, October 4, 2006.
52. *Molecular genetics of Agenesis of the corpus callosum with peripheral neuropathy.* Department of Pharmacology/Toxicology Seminar Series, Wright State University. Dayton, USA. October 18, 2006.

Research Grants (selected)

Génome Canada : Leader: Identif. and charact. of genes involved in common dev. brain diseases; 17.8M$; Mar06/Apr10

NIH(USA): Co-PI : Pharmacogenomics of ACE inhibitor-assocaited angioedeme; $58,000; Jan05/Dec09

CIHR Co-PI: Genetic and in Vivo Studies to Define the Role of Alsin in ALS; $61,998; Apr03/Mar08

MDA(USA): PI: Screening genes critical for the dev. of motor neurons in ALS; $115,000; Jan06/Dec08

CIHR: PI: Invest. of the role of polyALA acc. in expanded CAG tract diseases; $184,679; Oct04/Sep07

CIHR: PI: Characterizing the gene responsibie for ACCPN; $169,712; Apr02/Mar07

CIHR: PI: Molecular genetic investigation of OPMD; $190,180; Apr02/Mar07

MDA(USA): PI: Identification and characterization of the ALS3 gene; $120,000; Jan05/Dec06

NIH(USA): Co-PI: Genetic Predictors of Comormid Depresseive Symptoms + CAD; $84,000; Aug04/Jul06

CIHR: PI: Molecular genetic characterization of HSANII; $100,000; Oct05/Mar06

TSA(USA): PI: Identification of genes predisposing to TS in the French-Canadian population; $75,500; Apr05/Mar06

NIH(USA): Co-PI: Familial Intracranial Aneurysm Study; $104,241; Aug02/Jul05

RIMUHC: PI: Study of environmental, lifestyle, medical, family history, and genetic factors involved in Parkinson's disease in the Quebec population; $15,000; Jan05/Dec05

Heart and Stroke: PI :

NIH(USA): PI: Etiology of Restless Syndrome,a sleep disorder. US$497,243; Aug99-Jul02

MDA(USA): PI: Investigation of the pathogenesis of Oculopharyngeal Muscular Dystrophy (OPMD). US$300,000; Jul02/Jun05

MDA(USA): PI: Identification of a new gene for autosomal dominant familial amyotrophic lateral sclerosis. US$330,000; Jan02-Dec04

CGDN: PI: Mapping and identification of a gene for a unique form of pure autosomal recessive ataxia in the Beauce region of Quebec. $84,630; Sep03/AUg05

Pharmacia (Pfizer): PI: Biobank. $4,000,000 Aug00/Feb05

RLS Association: PI: Dissecting genes involved in Restless Legs Syndrome in French-Canadian population with elevated prevalence; 30,000US$; Jul03/Jun05

CIHR: PI: Autism. 2000-2003 240,000$

CIHR: PI: Investigation of the role of polyalanine accumulation inexpandede CAG tract diseases. 514,275$Oct00/mar04;

Bristol-Meyer-Squibb. PI: Genetic studies of Acute Side Effectts associated with metalopeptidase inhibitor. $160,000; Jan01/Dec02

ALSA (USA). PI: Generation of mALS2CR6 KO mice. US$66,105; Jan01/Dec03

National Ataxia Foundation. PI: Genetics of recessive ataxia. US$34,000 Jan02/Dec02

Tourette Syndrome ASsocaition (USA); PI: Use of the French-Canadian population for the identification of genes

predisposing to Tourette Syndrome. US$75,000; Apr02/Mar03

APPENDIX B

Appendix B - Bibliography

A selection of publications relevant to the structure and function of sodium channel domains or particular amino acid residues.
All articles are available from PubMedCentral except those indicated with an asterisk (*).

Ahmed CM, Ware DH, Lee SC, Patten CD, Ferrer-Montiel AV, Schinder AF, McPherson JD, Wagner-McPherson CB, Wasmuth JJ, Evans GA. Primary structure, chromosomal localization, and functional expression of a voltage-gated sodium channel from human brain. Proc Natl Acad Sci U S A. **1992 Sep 1**; 89(17): 8220-8224.

Armstrong CM, Cota G. Calcium block of Na+ channels and its effect on closing rate. Proc Natl Acad Sci U S A. **1999 Mar 30**; 96(7): 4154-4157.

Auld* VJ, Goldin AL, Krafte DS, Catterall WA, Lester HA, Davidson N, Dunn RJ. A neutral amino acid change in segment IIS4 dramatically alters the gating properties of the voltage-dependent sodium channel. Proc Natl Acad Sci U S A. **1990 Jan**;87(1):323-7.

Balser JR, Nuss HB, Chiamvimonvat N, Pérez-García MT, Marban E, Tomaselli GF. External pore residue mediates slow inactivation in mu 1 rat skeletal muscle sodium channels. J Physiol. **1996 Jul 15**; 494(Pt 2): 431-442.

Beckh S, Noda M, Lübbert H, Numa S. Differential regulation of three sodium channel messenger RNAs in the rat central nervous system during development. EMBO J. **1989 Dec 1**; 8(12): 3611-3616.

Belcher SM, Zerillo CA, Levenson R, Ritchie JM, Howe JR. Cloning of a sodium channel alpha subunit from rabbit Schwann cells. Proc Natl Acad Sci U S A. **1995 Nov 21**; 92(24): 11034-11038.

Bénitah JP, Ranjan R, Yamagishi T, Janecki M, Tomaselli GF, Marban E. Molecular motions within the pore of voltage-dependent sodium channels. Biophys J. **1997 Aug**; 73(2): 603-613.

Bénitah JP, Tomaselli GF, Marban E. Adjacent pore-lining residues within sodium channels identified by paired cysteine mutagenesis. Proc Natl Acad Sci U S A. **1996 Jul 9**; 93(14): 7392-7396.

Böhle T, Benndorf K. Voltage-dependent properties of three different gating modes in single cardiac Na+ channels. Biophys J. **1995 Sep**; 69(3): 873-882.

Chahine M, Sirois J, Marcotte P, Chen L, Kallen RG. Extrapore residues of the S5-S6 loop of domain 2 of the voltage-gated skeletal muscle sodium channel (rSkM1) contribute to the mu-conotoxin GIIIA binding site. Biophys J. **1998 Jul**; 75(1): 236-246.

Cherbavaz DB. Trimethyloxonium modification of batrachotoxin-activated Na channels alters functionally important protein residues. Biophys J. **1995 Apr**; 68(4): 1337-1346.

Chiamvimonvat N, Pérez-García MT, Tomaselli GF, Marban E. Control of ion flux and selectivity by negatively charged residues in the outer mouth of rat sodium channels. J Physiol. **1996 Feb 15**; 491(Pt 1): 51-59.

Cooper EC, Jan LY. Ion channel genes and human neurological disease: Recent progress, prospects, and challenges. Proc Natl Acad Sci U S A. **1999 Apr 27**; 96(9): 4759-4766.

Dib-Hajj SD, Tyrrell L, Black JA, Waxman SG. NaN, a novel voltage-gated Na channel, is expressed preferentially in peripheral sensory neurons and down-regulated after axotomy. Proc Natl Acad Sci U S A. **1998 Jul 21**; 95(15): 8963-8968.

Dudley SC Jr, Todt H, Lipkind G, Fozzard HA. A mu-conotoxin-insensitive Na+ channel mutant: possible localization of a binding site at the outer vestibule. Biophys J. **1995 Nov**; 69(5): 1657-1665.

Favre I, Moczydlowski E, Schild L. On the structural basis for ionic selectivity among Na+, K+, and Ca2+ in the voltage-gated sodium channel. Biophys J. **1996 Dec**; 71(6): 3110-3125.

Featherstone DE, Richmond JE, Ruben PC. Interaction between fast and slow inactivation in Skm1 sodium channels. Biophys J. **1996 Dec**; 71(6): 3098-3109.

Gautron S, Dos Santos G, Pinto-Henrique D, Koulakoff A, Gros F, Berwald-Netter Y. The glial voltage-gated sodium channel: cell- and tissue-specific mRNA expression. Proc Natl Acad Sci U S A. **1992 Aug 1**; 89(15): 7272-7276.

George AL Jr, Knittle TJ, Tamkun MM. Molecular cloning of an atypical voltage-gated sodium channel expressed in human heart and uterus: evidence for a distinct gene family. Proc Natl Acad Sci U S A. **1992 Jun 1**; 89(11): 4893-4897.

Hanna WJ, Tsushima RG, Sah R, McCutcheon LJ, Marban E, Backx PH. The equine periodic paralysis Na+ channel mutation alters molecular transitions between the open and inactivated states. J Physiol. **1996 Dec 1;** 497(Pt 2): 349-364.

Heginbotham L. Revisiting the ionic selectivity of Na+ channels. Biophys J. **1996 Dec**; 71(6): 2916-2918.

Kayano* T, Noda M, Flockerzi V, Takahashi H, Numa S. Primary structure of rat brain sodium channel III deduced from the cDNA sequence. FEBS Lett. **1988 Feb 8**;228(1):187-94.

Kellenberger S, Gautschi I, Schild L. A single point mutation in the pore region of the epithelial Na+ channel changes ion selectivity by modifying molecular sieving. Proc Natl Acad Sci U S A. **1999 Mar 30**; 96(7): 4170-4175.

Klugbauer N, Lacinova L, Flockerzi V, Hofmann F. Structure and functional expression of a new member of the tetrodotoxin-sensitive voltage-activated sodium channel family from human neuroendocrine cells. EMBO J. **1995 Mar 15**; 14(6): 1084-1090.

Lawrence JH, Orias DW, Balser JR, Nuss HB, Tomaselli GF, O'Rourke B, Marban E. Single-channel analysis of inactivation-defective rat skeletal muscle sodium channels containing the F1304Q mutation. Biophys J. **1996 Sep**; 71(3): 1285-1294.

Lerche H, Peter W, Fleischhauer R, Pika-Hartlaub U, Malina T, Mitrovic N, Lehmann-Horn F. Role in fast inactivation of the IV/S4-S5 loop of the human muscle Na+ channel probed by cysteine mutagenesis. J Physiol. **1997 Dec 1**; 505(Pt 2): 345-352.

Li RA, Tsushima RG, Kallen RG, Backx PH. Pore residues critical for mu-CTX binding to rat skeletal muscle Na+ channels revealed by cysteine mutagenesis. Biophys J. **1997 Oct**; 73(4): 1874-1884.

Lilly M, Kreber R, Ganetzky B, Carlson JR. Evidence That the Drosophila Olfactory Mutant Smellblind Defines a Novel Class of Sodium Channel Mutation. Genetics. **1994 Mar**; 136(3): 1087-1096.

Linford NJ, Cantrell AR, Qu Y, Scheuer T, Catterall WA. Interaction of batrachotoxin with the local anesthetic receptor site in transmembrane segment IVS6 of the voltage-gated sodium channel. Proc Natl Acad Sci U S A. **1998 Nov 10**; 95(23): 13947-13952.

Lipkind GM, Fozzard HA. A structural model of the tetrodotoxin and saxitoxin binding site of the Na+ channel. Biophys J. **1994 Jan**; 66(1): 1-13.

McPhee JC, Ragsdale DS, Scheuer T, Catterall WA. A mutation in segment IVS6 disrupts fast inactivation of sodium channels. Proc Natl Acad Sci U S A. **1994 Dec 6**; 91(25): 12346-12350.

Noda* M, Ikeda T, Kayano T, Suzuki H, Takeshima H, Kurasaki M, Takahashi H, Numa S. Existence of distinct sodium channel messenger RNAs in rat brain. Nature. **1986 Mar 13-19**;320(6058):188-92.

Noda* M, Ikeda T, Suzuki H, Takeshima H, Takahashi T, Kuno M, Numa S. Expression of functional sodium channels from cloned cDNA. Nature. **1986 Aug 28-Sep 3**;322(6082):826-8.

Noda* M, Numa S. Structure and function of sodium channel. J Recept Res. **1987**;7(1-4):467-97.

Noda* M, Shimizu S, Tanabe T, Takai T, Kayano T, Ikeda T, Takahashi H, Nakayama H, Kanaoka Y, Minamino N, et al. Primary structure of Electrophorus electricus sodium channel deduced from cDNA sequence. Nature. **1984 Nov 8-14;**312(5990):121-7.

Noda* M, Suzuki H, Numa S, Stuhmer W. A single point mutation confers tetrodotoxin and saxitoxin insensitivity on the sodium channel II. FEBS Lett. **1989 Dec 18**;259(1):213-6.

Numa* S, Noda M. Molecular structure of sodium channels. Ann N Y Acad Sci. **1986**;479:338-55.

Numa* S. Molecular basis for the function of ionic channels. Biochem Soc Symp. **1986**;52:119-43. Review.

Ogata N, Tatebayashi H. Kinetic analysis of two types of Na+ channels in rat dorsal root ganglia. J Physiol. **1993 Jul**; 466: 9-37.

Olivera BM. E.E. Just Lecture, 1996: Conus Venom Peptides, Receptor and Ion Channel Targets, and Drug Design: 50 Million Years of Neuropharmacology. Mol Biol Cell. **1997 Nov**; 8(11): 2101-2109.

Pérez-García MT, Chiamvimonvat N, Marban E, Tomaselli GF. Structure of the sodium channel pore revealed by serial cysteine mutagenesis. Proc Natl Acad Sci U S A. **1996 Jan 9**; 93(1): 300-304.

Pérez-García MT, Chiamvimonvat N, Ranjan R, Balser JR, Tomaselli GF, Marban E. Mechanisms of sodium/calcium selectivity in sodium channels probed by cysteine mutagenesis and sulfhydryl modification. Biophys J. **1997 Mar**; 72(3): 989-996.

Pusch* M, Noda M, Stuhmer W, Numa S, Conti F. Single point mutations of the sodium channel drastically reduce the pore permeability without preventing its gating. Eur Biophys J. **1991**;20(3):127-33.

Ragsdale DS, McPhee JC, Scheuer T, Catterall WA. Molecular determinants of state-dependent block of Na+ channels by local anesthetics. Science. **1994 Sep 16**;265(5179):1724-8.

Richmond JE, VanDeCarr D, Featherstone DE, George AL Jr, Ruben PC. Defective fast inactivation recovery and deactivation account for sodium channel myotonia in the I1160V mutant. Biophys J. **1997 Oct**; 73(4): 1896-1903.

Rose MR. Neurological channelopathies: Dysfunctional ion channels may cause many neurological diseases. BMJ. **1998 Apr 11**; 316(7138): 1104-1105.

Sarkar SN, Adhikari A, Sikdar SK. Kinetic characterization of rat brain type IIA sodium channel alpha-subunit stably expressed in a somatic cell line. J Physiol. **1995 Nov 1;** 488(Pt 3): 633-645.

Satin J, Limberis JT, Kyle JW, Rogart RB, Fozzard HA. The saxitoxin/tetrodotoxin binding site on cloned rat brain IIa Na channels is in the transmembrane electric field. Biophys J. **1994 Sep**; 67(3): 1007-1014.

Singh C, Sankararamakrishnan R, Subramaniam S, Jakobsson E. Solvation, water permeation, and ionic selectivity of a putative model for the pore region of the voltage-gated sodium channel. Biophys J. **1996 Nov**; 71(5): 2276-2288.

Smith MR, Goldin AL. Interaction between the sodium channel inactivation linker and domain III S4-S5. Biophys J. **1997 Oct**; 73(4): 1885-1895.

Solaro CR, Ding JP, Li ZW, Lingle CJ. The cytosolic inactivation domains of BKi channels in rat chromaffin cells do not behave like simple, open-channel blockers. Biophys J. **1997 Aug**; 73(2): 819-830.

Stuhmer* W, Conti F, Suzuki H, Wang XD, Noda M, Yahagi N, Kubo H, Numa S. Structural parts involved in activation and inactivation of the sodium channel. Nature. **1989 Jun 22**;339(6226):597-603.

Stuhmer* W, Methfessel C, Sakmann B, Noda M, Numa S. Patch clamp characterization of sodium channels expressed from rat brain cDNA. Eur Biophys J. **1987**;14(3):131-8.

Sunami A, Dudley SC Jr, Fozzard HA. Sodium channel selectivity filter regulates antiarrhythmic drug binding. Proc Natl Acad Sci U S A. **1997 Dec 9**; 94(25): 14126-14131.

Suzuki* H, Beckh S, Kubo H, Yahagi N, Ishida H, Kayano T, Noda M, Numa S. Functional expression of cloned cDNA encoding sodium channel III. FEBS Lett. **1988 Feb 8**;228(1):195-200.

Toledo-Aral JJ, Moss BL, He ZJ, Koszowski AG, Whisenand T, Levinson S, Wolf J, Silos-Santiago I, Halegoua S, Mandel G. Identification of PN1, a predominant voltage-dependent sodium channel expressed principally in peripheral neurons. Proc Natl Acad Sci U S A. **1997 Feb 18**; 94(4): 1527-1532.

Tomaselli GF, Chiamvimonvat N, Nuss HB, Balser JR, Pérez-García MT, Xu RH, Orias DW, Backx PH, Marban E. A mutation in the pore of the sodium channel alters gating. Biophys J. **1995 May**; 68(5): 1814-1827.

Vandenberg CA, Bezanilla F. A sodium channel gating model based on single channel, macroscopic ionic, and gating currents in the squid giant axon. Biophys J. **1991 Dec**; 60(6): 1511-1533.

Vassilev P, Scheuer T, Catterall WA. Inhibition of inactivation of single sodium channels by a site-directed antibody. Proc Natl Acad Sci U S A. **1989 Oct**; 86(20): 8147-8151.

Wang D, Yazawa K, George A Jr, Bennett P. Characterization of human cardiac Na+ channel mutations in the congenital long QT syndrome. Proc Natl Acad Sci U S A. **1996 Nov 12**; 93(23): 13200-13205.

Wang DW, Yazawa K, Makita N, George AL Jr, Bennett PB. Pharmacological targeting of long QT mutant sodium channels. J Clin Invest. **1997 Apr 1**; 99(7): 1714-1720.

Wang SY, Wang GK. A mutation in segment I-S6 alters slow inactivation of sodium channels. Biophys J. **1997 Apr**; 72(4): 1633-1640.

West JW, Numann R, Murphy BJ, Scheuer T, Catterall WA. Phosphorylation of a conserved protein kinase C site is required for modulation of Na+ currents in transfected Chinese hamster ovary cells. Biophys J. **1992 Apr**; 62(1): 31-33.

Yamagishi T, Janecki M, Marban E, Tomaselli GF. Topology of the P segments in the sodium channel pore revealed by cysteine mutagenesis. Biophys J. **1997 Jul**; 73(1): 195-204.

Yang N, George AL Jr, Horn R. Probing the outer vestibule of a sodium channel voltage sensor. Biophys J. **1997 Nov**; 73(5): 2260-2268.

Yang N, Ji S, Zhou M, Ptácek LJ, Barchi RL, Horn R, George AL Jr. Sodium channel mutations in paramyotonia congenita exhibit similar biophysical phenotypes in vitro. Proc Natl Acad Sci U S A. **1994 Dec 20**; 91(26): 12785-12789.

APPENDIX C

Appendix C - Alignments

Sequence alignment of human sodium channel alpha subunits available prior to submission of the provisional patent application in November 1999 (see below) and priority using *ClustalW*. Conserved TM domains are indicated with <<< >>> symbols. The location of Ser1773Tyr mutation in SCN1A is indicated with #.

```
hSCN1A              ---MEQTVLVPPGPDSFNFFTRESLAAIERRIAEEKAKNPKPD----KKDDDENGPKPNS 53
hSCN5A-M77235       ----MANFLLPRGTSSFRRFTRESLAAIEKRMAEKQARGSTTLQESREGLPEEEAPRPQL 56
hSCN10A-AF117907    ----MEFPIGSLETNNFRRFTPESLVEIEKQIAAKQG-TKKAREKHREQKDQEEKPRPQL 55
hSCN4A-M81758       MARPSLCTLARLGPECLRPFTRESLAAIEQRAVEEEA----RLQRNKQMEIEEPERKPRS 56
hSCN2A              ---MAQSVLVPPGPDSFRFFTRESLAAIEQRIAEEKAKRPKQER---KDEDDENGPKPNS 54
hSCN3A              ---MAQALLVPPGPESFRLFTRESLAAIEKRAAEEKAKKPKKE----QDNDDENKPKPNS 53
hSCN8A-AB027567     ---MAARLLAPPGPDSFKPFTPESLANIERRIAESKLKKPPKADGSHREDDEDSKPKPNS 57
hSCN9A-X82835       -----MAMLPPPGPQSFVHFTKQSLALIEQRIAERKSKEPKEE----KKDDDEEAPKPSS 51
hSCN6A-M91556       -------MLASPEPKGLVPFTKESFELIKQHIAKTHN-----------EDHEEEDLKPNP 42
                    :         :     .. :  **  :*:  *::: .  .              ::   :*

hSCN1A              DLEAGKNLPFIYGDIPPEMVSEPLEDLDPYYINKK-TFIVLNKGKAIFRFSATSALYILT 112
hSCN5A-M77235       DLQASKKLPDLYGNPPQELIGEPLEDLDPFYSTQK-TFIVLNKGKTIFRFSATNALYVLS 115
hSCN10A-AF117907    DLKACNQLPKFYGELPAELIGEPLEDLDPFYSTHR-TFMVLNKGRTISRFSATRALWLFS 114
hSCN4A-M81758       DLEAGKNLPMIYGDPPPEVIGIPLEDLDPYYSNKK-TFIVLNKGKAIFRFSATPALYLLS 115
hSCN2A              DLEAGKSLPFIYGDIPPEMVSVPLEDLDPYYINKK-TFIVLNKGKAISRFSATPALYILT 113
hSCN3A              DLEAGKNLPFIYGDIPPEMVSEPLEDLDPYYINKK-TFIVMNKGKAISRFSATSALYILT 112
hSCN8A-AB027567     DLEAGKSLPFIYGDIPQGLVAVPLEDFDPYYLTQK-TFVVLNRGKTLFRFSATPALYILS 116
hSCN9A-X82835       DLEAGKQLPFIYGDIPPGMVSEPLEDLDPYYADKK-TFIVLNKGKTIFRFNATPALYMLS 110
hSCN6A-M91556       DLEVGKKLPFIYGNLSQGMVSEPLEDVDPYYYKKKNTFIVLNKNRTIFRFNAASILCTLS 102
                    **:. :.** :**: .  ::  ****.**:*  :: **:*:*:.::: **.*:  *  ::

                                 <<<<<  I-S1  >>>>>>>>>>>       <<<<<<< I-S2 >>>>
hSCN1A              PFNPLRKIAIKILVHSLFSMLIMCTILTNCVFMTMSNPPDWTKNVEYTFTGIYTFESLIK 172
hSCN5A-M77235       PFHPVRRAAVKILVHSLFNMLIMCTILTNCVFMAQHDPPPWTKYVEYTFTAIYTFESLVK 175
hSCN10A-AF117907    PFNLIRRTAIKVSVHSWFSLFITVTILVNCVCMTRTDLP---EKIEYVFTVIYTFEALIK 171
hSCN4A-M81758       PFSVVRRGAIKVLIHALFSMFIMITILTNCVFMTMSDPPPWSKNVEYTFTGIYTFESLIK 175
hSCN2A              PFNPIRKLAIKILVHSLFNMLIMCTILTNCVFMTMSNPPDWTKNVEYTFTGIYTFESLIK 173
hSCN3A              PLNPVRKIAXKILVHSLFSMLIMCTILTNCVFMTLSNPPDWTKNVEYTFTGIYTFESLIK 172
hSCN8A-AB027567     PFNLIRRIAIKILIHSVFSMIIMCTILTNCVFMTFSNPPDWSKNVEYTFTGIYTFESLVK 176
hSCN9A-X82835       PFSPLRRISIKILVHSLFSMLIMCTILTNCIFMTMNNPPDWTKNVEYTFTGIYTFESLVK 170
hSCN6A-M91556       PFNCIRRTTIKVLVHPFFQLFILISVLIDCVFMSLTNLPKWRPVLENTLLGIYTFEILVK 162
                    *:  :*: : *: :*. *.::*  ::* :*: *:   : *       :* .:  ***** *:*

                    >>>                 <<<<<< I-S3 >>>>>>>      <<<<<< I-S4 >>>>>>>
hSCN1A              IIARGFCLEDFTFLRDPWNWLDFTVITFAYVTEFVDLGNVSALRTFRVLRALKTISVIPG 232
hSCN5A-M77235       ILARAFCLHAFTFLRDPWNWLDFSVIIMAYTTEFVDLGNVSALRTFRVLRALKTISVISG 235
hSCN10A-AF117907    ILARGFCLNEFTYLRDPWNWLDFSVITLAYVGTAIDLRGISGLRTFRVLRALKTVSVIPG 231
hSCN4A-M81758       ILARGFCVDDFTFLRDPWNWLDFSVIMMAYLTEFVDLGNISALRTFRVLRALKTITVIPG 235
hSCN2A              ILARGFCLEDFTFLRDPWNWLDFTVITFAYVTEFVDLGNVSALRTFRVLRALKTISVIPG 233
hSCN3A              ILARGFCLEDFTFLRDPWNWLDFSVIVMAYVTEFVDLGNVSALRTFRVLRALKTISVIPG 232
hSCN8A-AB027567     IIARGFCIDGFTFLRDPWNWLDFSVIMMAYITEFVNLGNVSALRTFRVLRALKTISVIPG 236
hSCN9A-X82835       ILARGFCVGEFTFLRDPWNWLDFVVIVFAYLTEFVNLGNVSALRTFRVLRALKTISVIPG 230
hSCN6A-M91556       LFARGVWAGSFSFLGDPWNWLDFSVTVFEVIIRYSPLDFIPTLQTARTLRILKIIPLNQG 222
                    ::**..     *::* ******** *   :           *  :. *:* *.** ** :.:  *

                    >                  <<<<<<< I-S5 >>>>>>>>>>>
hSCN1A              LKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCIQWPPTNASLEEHSI 292
hSCN5A-M77235       LKTIVGALIQSVKKLADVMVLTVFCLSVFALIGLQLFMGNLRHKCVRNFTALNGT----- 290
hSCN10A-AF117907    LKVIVGALIHSVKKLADVTILTIFCLSVFALVGLQLFKGNLKNKCVKNDMAVNET----- 286
hSCN4A-M81758       LKTIVGALIQSVKKLSDVMILTVFCLSVFALVGLQLFMGNLRQKCVRWPPPFNDTNTTWY 295
hSCN2A              LKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCLQWPPDNSSFEINIT 293
hSCN3A              LKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCLQWPPSDSAFETNTT 292
hSCN8A-AB027567     LKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCVVWP----------- 285
hSCN9A-X82835       LKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLKHKCFRNSLE--------- 281
hSCN6A-M91556       LKSLVGVLIHCLKQLIGVIILTLFFLSIFSLIGMGLFMGNLKHKCFRWP----------- 271
                    ** :**.**:.:*:* .* :**:* **:*:*:*: ** ***::**.
```

```
hSCN1A              EKN---------------------ITVNYNGTLINETVFEFDWKSYIQDSRYHYFLEGFL 331
hSCN5A-M77235       -----------------------------NGSVEADGLVWESLDLYLSDPENYLLKNGTS 321
hSCN10A-AF117907    -----------------------------TNYSSHR------------KPDIYINKRGTS 305
hSCN4A-M81758       SNDTWYGNDTWYGNEMWYGNDSWYANDTWNSHASWATNDTFDWDAYISDEGNFYFLEGSN 355
hSCN2A              SFFN--------------------NSLDGNGTTFNRTVSIFNWDEYIEDKSHFYFLEGQN 333
hSCN3A              SYFN--------------------GTMDSNGTFVNVTMSTFNWKDYIGDDSHFYVLDGQK 332
hSCN8A-AB027567     --------------------------INFNESYLENGTKGFDWEEYINNKTNFYTVPGML 319
hSCN9A-X82835       -----------------------------NNETLESIMNTLESEEDFR--KYFYYLEGSK 310
hSCN6A-M91556       -----------------------------QENENETLHNRTGNPYYIRETENFYYLEGEK 302
                              :                              :     .     *

hSCN1A              DALLCGNSSDAGQCPEGYMCVKAGKNPNYGYTSFDTFSWAFLSLFRLMTQDFWENLYQLT 391
hSCN5A-M77235       DVLLCGNSSDAGTCPEGYRCLKAGENPDHGYTSFDSFAWAFLALFRLMTQDCWERLYQQT 381
hSCN10A-AF117907    DPLLCGNGSDSGHCPDGYICLKTSDNPDFNYTSFDSFAWAFLSLFRLMTQDSWERLYQQT 365
hSCN4A-M81758       DALLCGNSSDAGHCPKGYECIKTGRNPNYGYTSYDTFSWAFLALFRLMTQDYWENLFQLT 415
hSCN2A              DALLCGNSSDAGQCPEGYICVKAGRNPNYGYTSFDTFSWAFLSLFRLMTQDFWENLYQLT 393
hSCN3A              DPLLCGNGSDAGQCPEGYICVKAGRNPNYGYTSFDTFSWAFLSLFRLMTQDYWENLYQLT 392
hSCN8A-AB027567     EPLLCGNSSDAGQCPEGYQCMKAGRNPNYGYTSFDTFSWAFLALFRLMTQDYWENLYQLT 379
hSCN9A-X82835       DALLCGFSTDSGQCPEGYTCVKIGRNPDYGYTSFDTFSWAFLALFRLMTQDYWENLYQQT 370
hSCN6A-M91556       YALLCGNFTDAGQCPEGYVCVKAGINPDQGFTNFDSFGWALFALFRLMAQDYPEVLYHLI 362
                      ****  :*:* **.** *:*  .  **:  .:*.:*:*.**:::*****:**  * *::

                       <<<<<< I-S6 >>>>>>>>>>>>>>
hSCN1A              LRAAGKTYMIFFVLVIFLGSFYLINLILAVVAMAYEEQNQATLEEAEQKEAEFQQMIEQL 451
hSCN5A-M77235       LRSAGKIYMIFFMLVIFLGSFYLVNLILAVVAMAYEEQNQATIAETEEKEKRFQEAMEML 441
hSCN10A-AF117907    LRTSGKIYMIFFVLVIFLGSFYLVNLILAVVTMAYEEQNQATTDEIEAKEKKFQEALEML 425
hSCN4A-M81758       LRAAGKTYMIFFVVIIFLGSFYLINLILAVVAMAYAEQNEATLAEDKEKEEEFQQMLEKF 475
hSCN2A              LRAAGKTYMIFFVLVIFLGSFYLINLILAVVAMAYEEQNQATLEEAEQKEAEFQQMLEQL 453
hSCN3A              LRAAGKTYMIFFVLVIFLGSFYLVNLILAVVAMAYEGQNQATLEEAEQKEAEFQQMLEQL 452
hSCN8A-AB027567     LRAAGKTYMIFFVLVIFVGSFYLVNLILAVVAMAYEEQNQATLEEAEQKEAEFKAMLEQL 439
hSCN9A-X82835       LRAAGKTYMIFFVVVIFLGSFYLINLILAVVAMAYEEQNQANIEEAKQKELEFQQMLDRL 430
hSCN6A-M91556       LYASGKVYMIFFVVVSFLFSFYMASLFLGILAMAYEEEKQRVGEISKKIEPKFQQTGKEL 422
                    *  ::** *****::: *: ***: .*:*.:::***  :::        :  * .*:   . :

hSCN1A              KKQQEAAQQAATAT--ASEHSREPSAAGRLS----DSSSEASKLSSKSAKERRNRRKKRK 505
hSCN5A-M77235       KKEHEALTIRGVDT--------------------VSRSSLEMSPLAPVNSHERRSKRRKR- 481
hSCN10A-AF117907    RKEQEVLAALGIDT--------------------TSLHSHNGSPLTSKNASERRHRIKPR- 465
hSCN4A-M81758       KKHQEEL----------------------------------------------------- 482
hSCN2A              KKQQEEAQAAAAAASAESRDFSGAGGIGVFS----ESSSVASKLSSKSEKELKNRRKKKK 509
hSCN3A              KKQQEEAQAVAAAS-AASRDFSGIGGLGELL----ESSSEASKLSSKSAKEWRNRRKKRR 507
hSCN8A-AB027567     KKQQEEAQAAAMATSAGTVSEDAIEEEGEEGGGSPRSSSEISKLSSKSAKERRNRRKKRK 499
hSCN9A-X82835       KKEQEEAEAIAAAA-AEYTSIRRSRIMGLSE-----SSSETSKLSSKSAKERRNRRKKKN 484
hSCN6A-M91556       QEGNETDEAK-------------------------------------------------- 432
                    ::  :*

hSCN1A              QKEQSGGEEKDEDE-FQKSESEDSIRRKGFRFSIEGNRLTYEKRYSSPHQSLLSIRGSLF 564
hSCN5A-M77235       ---MSSGTEECGEDRLPKSDSEDGPRAMNH-------------------LSLTRGLSRTS 519
hSCN10A-AF117907    ---VSEGSTE--DNKSPRSDPYN-QRRMSF-------------------LGLASG----- 495
hSCN4A-M81758       ------------------------EKAKAA-------------------QALEGG----- 494
hSCN2A              QKEQSGEEEKNDR--VLKSESEDSIRRKGFRFSLEGSRLTYEKRFSSPHQSLLSIRGSLF 567
hSCN3A              QREHLEGNNKGERDSFPKSESEDSVKRSSFLFSMDGNRLTSDKKFCSPHQSLLSIRGSLF 567
hSCN8A-AB027567     QKELSEGEEKGDPEKVFKSESEDGMRRKAFRLPD--NRIG--RKFSIMNQSLLSIPGSPF 555
hSCN9A-X82835       QKKLSSGEEKGDAEKLSKSESEDSIRRKSFHLGVEGHRRAHEKRLSTPNQSPLSIRGSLF 544
hSCN6A-M91556       ------------------------------------------------------------

hSCN1A              SPRRNSRTSLFSFRG--RAKDVGSENDFADDEHSTFEDNESRRDSLFVPRRHGERRNSNL 622
hSCN5A-M77235       MKPRSSRGSIFTFRR----RDLGSEADFADDENSTARESESHHTSLLVPWPLRRTSAQGQ 575
hSCN10A-AF117907    -KRRASHGSVFHFRSP--GRDISLPEGVTDDG-VFPGDHESHRGSLLLGG------GAGQ 545
hSCN4A-M81758       ------------------------------------------------------------
hSCN2A              SPRRNSRASLFSFRG--RAKDIGSENDFADDEHSTFEDNDSRRDSLFVPHRHGERRHSNV 625
hSCN3A              SPRRNSKTSIFSFRG--RAKDVGSENDFADDEHSTFEDSESRRDSLFVPHRHGERRNS-- 623
hSCN8A-AB027567     LSRHNSKSSIFSFRGPGRFRDPGSENEFADDEHSTVEESEGRRDSLFIPIRARERRSSYS 615
hSCN9A-X82835       SARRSSRTSLFSFKG--RGRDIGSETEFADDEHSIFGDNESRRGSLFVPHRPQERRSSNI 602
hSCN6A-M91556       ------------------------------------------------------------
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hSCN1A              -----SQTSPSSRMLAVFPANGKMHSTVDCNGVVSLVGGPSVPTSPVGQLLPEVIIDKPA 677
hSCN5A-M77235       P--------SPGTSAPGHALHGKKNSTVDCNGVVSLLGAGDPEATSPGSHLLR----PVM 623
hSCN10A-AF117907    Q--------GPLPRSP-------------------LPQPSNPDSRHGEDEHQP----PPT 574
hSCN4A-M81758       ---------------------------------------EADGDPAHGKDCN--------- 507
hSCN2A              -----SQASRASRVLPILPMNGKMHSAVDCNGVVSLVGGPSTLTSAGQLLP--------- 671
hSCN3A              ------------------------------------------------------------
hSCN8A-AB027567     GYSGYSQGSRSSRIFPSLRRSVKRNSTVDCNGVVSLIGGPGSHIGGRLLP---------- 665
hSCN9A-X82835       S--------QASRSPPMLPVNGKMHSAVDCNGVVSLVDGRSALMLPNGQLLPEVIIDKAT 654
hSCN6A-M91556       ------------------------------------------------------------

hSCN1A              TDDNGTTTETEMRKRRSSSFHVSMDFLE---DPSQRQRAMSIASILTNT-VEELEESRQK 733
hSCN5A-M77235       LEHPPDTTTPSEEPGGPQMLTSQAPCVDGFEEPGARQRALSAVSVLTSA-LEELEESRHK 682
hSCN10A-AF117907    SELAPGAVDVSAFDAGQKKTFLSAEYLD---EPFRAQRAMSVVSIITSV-LEELEESEQK 630
hSCN4A-M81758       -----GSLDTSQGEKG-----------------APRQSGSGDSGISDA-MEELEEAHQK 543
hSCN2A              ---EGTTTETEIKKRRSSSYHVSMDLLE---DPTSRQRAMSIASILTNT-MEELEESRQK 724
hSCN3A              ---NGTTTETEVKKRRLSSYQISMEMLE---DSSGRQRAVSIASILTNT-MEELEESRQK 676
hSCN8A-AB027567     ----EATTEVEIKKKGPGSLLVSMDQLA---SYGRKDRINSIMSVVTNTLVEELEESQRK 718
hSCN9A-X82835       SD-DSGTTNQIHKKRRCSSYLLSEDMLN---DPNLRQRAMSRASILTNT-VEELEESRQK 709
hSCN6A-M91556       ------TIQIEMKKRS-----------------PISTDTSLDVLEDATLRHKEELEKSKKI 470
                          :                                .   .   :    ****::.:

                                                 <<<<<< II-S1 >>>>>>>>>>>>
hSCN1A              CPPCWYKFSNIFLIWDCSPYWLKVKHVVNLVVMDPFVDLAITICIVLNTLFMAMEHYPMT 793
hSCN5A-M77235       CPPCWNRLAQRYLIWECCPLWMSIKQGVKLVVMDPFTDLTITMCIVLNTLFMALEHYNMT 742
hSCN10A-AF117907    CPPCLTSLSQKYLIWDCCPMWVKLKTILFGLVTDPFAELTITLCIVVNTIFMAMEHHGMS 690
hSCN4A-M81758       CPPWWYKCAHKVLIWDCCAPWLKFKNIIHLIVMDPFVDLGITICIVLNTLFMAMEHYPMT 603
hSCN2A              CPPCWYKFANMCLIWDCCKPWLKVKHLVNLVVMDPFVDLAITICIVLNTLFMAMEHYPMT 784
hSCN3A              CPPCWYRFANVFLIWDCCDAWLKVKHLVNLIVMDPFVDLAITICIVLNTLFMAMEHYPMT 736
hSCN8A-AB027567     CPPCWYKFANTFLIWECHPYWIKLKEIVNLIVMDPFVDLAITICIVLNTLFMAMEHHPMT 778
hSCN9A-X82835       CPPWWYRFAHKFLIWNCSPYWIKFKKCIYFIVMDPFVDLAITICIVLNTLFMAMEHHPMT 769
hSCN6A-M91556       CPLYWYKFAKTFLIWNCSPCWLKLKEFVHRIIMAPFTDLFLIICIILNVCFLTLEHYPMS 530
                    **       ::  ***:*   *:..*  :  ::  **.:* : :**::*. *:::**: *:

                          <<<<<<<< II-S2 >>>>>>>>>       <<<<<<<< II-S3 >>>>>
hSCN1A              DHFNNVLTVGNLVFTGIFTAEMFLKIIAMDPYYYFQEGWNIFDGFIVTLSLVELGLANVE 853
hSCN5A-M77235       SEFEEMLQVGNLVFTGIFTAEMTFKIIALDPYYYFQQGWNIFDSIIVILSLMELGLSRMS 802
hSCN10A-AF117907    PTFEAMLQIGNIVFTIFFTAEMVFKIIAFDPYYYFQKKWNIFDCIIVTVSLLELGVAKKG 750
hSCN4A-M81758       EHFDNVLTVGNLVFTGIFTAEMVLKLIAMDPYEYFQQGWNIFDSIIVTLSLVELGLANVQ 663
hSCN2A              EQFSSVLSVGNLVFTGIFTAEMFLKIIAMDPYYYFQEGWNIFDGFIVSLSLMELGLANVE 844
hSCN3A              EQFSSVLTVGNLVFTGIFTAEMVLKIIAMDPYYYFQEGWNIFDGIIVSLSLMELGLSNVE 796
hSCN8A-AB027567     PQFEHVLAVGNLVFTGIFTAEMFLKLIAMDPYYYFQEGWNIFDGFIVSLSLMELSLADVE 838
hSCN9A-X82835       EEFKNVLAIGNLVFTGIFAAEMVLKLIAMDPYEYFQVGWNIFDSLIVTLSLVELFLADVE 829
hSCN6A-M91556       KQTNTLLNIGNLVFIGIFTAEMIFKIIAMHPYGYFQVGWNIFDSMIVFHGLIELCLANVA 590
                       . :* :**:**  :*:*** :*:**:.** ***  ***** :**   .*:** ::

                        <<<<<<< II-S4 >>>>>>>         <<<<< II-S5 >>>>>>>>>
hSCN1A              GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 913
hSCN5A-M77235       NLSVLRSFRLLRVFKLAKSWPTLNTLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 862
hSCN10A-AF117907    SLSVLRSFRLLRVFKLAKSWPTLNTLIKIIGNSVGALGNLTIILAIIVFVFALVGKQLLG 810
hSCN4A-M81758       GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 723
hSCN2A              GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 904
hSCN3A              GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 856
hSCN8A-AB027567     GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 898
hSCN9A-X82835       GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFG 889
hSCN6A-M91556       GMALLRLFRMLRIFKLGKYWPTFQILMWSLSNSWVALKDLVLLLFTFIFFSAAFGMKLFG 650
                    .:::** **:**:***.* ***:: *:  :.**  ** :*.::*  ::*. * .* :*:*

                                                                          <<<<<<
hSCN1A              KSYKDCVCKIASD-CQLPRWHMNDFFHSFLIVFRVLCGEWIETMWDCMEVAGQAMCLTVF 972
hSCN5A-M77235       KNYSELRDSDSG---LLPRWHMMDFFHAFLIIFRILCGEWIETMWDCMEVSGQSLCLLVF 919
hSCN10A-AF117907    ENYRNNRKNISAPHEDWPRWHMHDFFHSFLIVFRILCGEWIENMWACMEVGQKSICLILF 870
hSCN4A-M81758       KSYKECVCKIALD-CNLPRWHMHDFFHSFLIVFRILCGEWIETMWDCMEVAGQAMCLTVF 782
hSCN2A              KSYKECVCKISND-CELPRWHMHDFFHSFLIVFRVLCGEWIETMWDCMEVAGQTMCLTVF 963
hSCN3A              KSYKECVCKINDD-CTLPRWHMNDFFHSFLIVFRVLCGEWIETMWDCMEVAGQTMCLIVF 915
hSCN8A-AB027567     KSYKECVCKINQD-CELPRWHMHDFFHSFLIVFRVLCGEWIETMWDCMEVAGQAMCLIVF 957
hSCN9A-X82835       KSYKECVCKINDD-CTLPRWHMNDFFHSFLIVFRVLCGEWIETMWDCMEVAGQAMCLIVY 948
hSCN6A-M91556       KNYEEFVCHIDKD-CQLPRWHMHDFFHSFLNVFRILCGEWVETLWDCMEVAGQSWCIPFY 709
                    :.* :              ***** ****:** :**:*****:*.:* ****. :: *: .:
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                    II-S6 >>>>>>>>>>>>>>
hSCN1A              MMVMVIGNLVVLNLFLALLLSSFSADNLAATDDDNEMNNLQIAVDRMHKGVAYVKRKIYE 1032
hSCN5A-M77235       LLVMVIGNLVVLNLFLALLLSSFSADNLTAPDEDREMNNLQLALARIQRGLRFVKRTTWD 979
hSCN10A-AF117907    LTVMVLGNLVVLNLFIALLLNSFSADNLTAPEDDGEVNNLQVALARIQ---VFGHRTKQA 927
hSCN4A-M81758       LMVMVIGNLVVLNLFLALLLSSFSADSLAASDEDGEMNNLQIAIGRIKLGIGFAKAFLLG 842
hSCN2A              MMVMVIGNLVVLNLFLALLLSSFSSDNLAATDDDNEMNNLQIAVGRMQKGIDFVKRKIRE 1023
hSCN3A              MLVMVIGNLVVLNLFLALLLSSFSSDNLAATDDDNEMNNLQIAVGRMQKGIDYVKNKMRE 975
hSCN8A-AB027567     MMVMVIGNLVVLNLFLALLLSSFSADNLAATDDDGEMNNLQISVIRIKKGVAWTKLKVHA 1017
hSCN9A-X82835       MMVMVIGNLVVLNLFLALLLSSFSSDNLTAIEEDPDANNLQIAVTRIKKGINYVKQTLRE 1008
hSCN6A-M91556       LMVILIGNLLVLYLFLALVS-SFSSCKDVTAEENNEAKNLQLAVARIKKGINYVLLKILC 768
                    : *:::***:** **:**:  ***; . .: ::: ; :***::: *::  : :

hSCN1A              FIQ-------------QSFIKKQKILDEIKPLDDLNNKKDSCMSNHT-AEIGKDLDYLKD 1078
hSCN5A-M77235       FCCGLLKHR--PQKPAALAAQGQLPSCIATPYSPPPPETEKVPPTRKETQFEEGEQPGQG 1037
hSCN10A-AF117907    LCSFFSRSCPFPQPKAEPELVVKLPLSSSKAENHIAANTARGSSGGLQAPRGPRDEHSDF 987
hSCN4A-M81758       LLHGKILSP-----------KDIMLSLGEADGAGEAGEAGETAPEDEKKEPPEEDLKKDNH 892
hSCN2A              FIQ-------------KAFVRKQKALDEIKPLEDLNNKKDSCISNHTTIEIGKDLNYLKD 1070
hSCN3A              CFQ-------------KAFFRKPKVIEIHE-----GNKIDSCMSNNTGIEISKELNYLRD 1017
hSCN8A-AB027567     FMQ-------------AHFKQRE--ADEVKPLDELYEKKANCIANHTGADIHRNGDFQKN 1062
hSCN9A-X82835       FIL-------------KAFSKKPKISREIRQAEDLNTKKENYISNHTLAEMSKGHNFLKE 1055
hSCN6A-M91556       KTQN-------------------VPKDTMDHVNEVYVKED--ISDHTLSELSNTQDFLKD 807
                                                                                .

hSCN1A              VNGITSGIGTGSSVEKYIIDESDYMSFINNPSLTVTVPIAVGESDFENLN---------- 1128
hSCN5A-M77235       TPGDPEPVCVPIAVAESDTDDQEEDE-ENSLGTEEESSKQQESQPVSGWPRGPPDSRTWS 1096
hSCN10A-AF117907    IANPTVWVSVPIAEGESDLDDLEDDGGEDAQSFQQEVIPKGQQEQLQQVERCG-DHLTPR 1046
hSCN4A-M81758       ILN-----HMGLADGPPSSLELDHLNFINNPYLTIQVPIASEESDLEMP----------- 936
hSCN2A              GNGTTSGIG--SSVEKYVVDESDYMSFINNPSLTVTVPIAVGESDFENLN---------- 1118
hSCN3A              GNGTTSGVGTGSSVEKYVIDENDYMSFINNPSLTVTVPIAVGESDFENLN---------- 1067
hSCN8A-AB027567     GNGTTSGIG--SSVEKYIIDE-DHMSFINNPNLTVRVPIAVGESDFENLN---------- 1109
hSCN9A-X82835       -KDKISGFG--SSVDKHLMEDSDGQSFIHNPSLTVTVPIAPGESDLENMN---------- 1102
hSCN6A-M91556       KEK--------SSGTEKNATENESQSLIPSPSVSETVPIASGESDIENLD---------- 849
                                 :          : :                       .. ..

hSCN1A              -------TEDFSSESDLEESKEKLNE----------SSSSSEGSTVDIGAPVE-EQPVVE 1170
hSCN5A-M77235       QVSATASSEAEASASQADWRQQWKAEPQAPGCGETPEDSCSEGSTADMTNTAELLEQIPD 1156
hSCN10A-AF117907    SPGTGTSSEDLAPSLGETWKDESVPQAPAEGVDDT---SSSEGSTVDCLDPEEILRKIPE 1103
hSCN4A-M81758       -------TEFETDTFSEPEDSKKPPQPLYDG-------NSSVCSTADYKPPEEDPEEQAE 982
hSCN2A              -------TEEFSSESDMEESKEKLN-----------ATSSSEGSTVDIGAPAEGEQPEVE 1160
hSCN3A              -------TEEFSSESELEESKEKLN-----------ATSSSEGSTVDVVLPREGEQAETE 1109
hSCN8A-AB027567     -------TEDVSSESDPEGSKDKLD-----------DTSSSEGSTIDIKPEVE-EVPVEQ 1150
hSCN9A-X82835       -------AEELSSDSDSEYSKVRLN-----------RSSSSECSTVDNPLPGEGEEAEAE 1144
hSCN6A-M91556       -------NKEIQSKSGDGGSKEKIKQ----------SSSSECSTVDIAISEEEEMFYGG 891
                            :              ,                 ..*   ** -      *

                                                         <<<<< III-S1 >>>
hSCN1A              PEETLE-PEACFTEGCVQRFKCCQINVEEGRGKQWWNLRRTCFRIVEHNWFETFIVFMIL 1229
hSCN5A-M77235       LGQDVKDPEDCFTEGCVRRCPCCAVDTTQAPGKVWWRLRKTCYHIVEHSWFETFIIFMIL 1216
hSCN10A-AF117907    LADDLEEPDDCFTEGCIRHCPCCKLDTTKSPWDVGWQVRKTCYRIVEHSWFESFIIFMIL 1163
hSCN4A-M81758       ENPEGEQPEECFTEACVQRWPCLYVDISQGRGKKWWTLRRACFKIVEHNWFETFIVFMIL 1042
hSCN2A              PEESLE-PEACFTEDCVRKFKCCQISIEEGKGKLWWNLRKTCYKIVEHNWFETFIVFMIL 1219
hSCN3A              PEDLKK-PEACFTEGCIKKFPFCQVSTEEGKGKIWWNLRKTCYSIVEHNWFETFIVFMIL 1168
hSCN8A-AB027567     PEEYLD-PDACFTEGCVQRFKCCQVNIEEGLGKSWWILRKTCFLIVEHNWFETFIIFMIL 1209
hSCN9A-X82835       PMNSDE-PEACFTDGCVRRFSCCQVNIESGKGKIWWNIRKTCYKIVEHSWFESFIVLMIL 1203
hSCN6A-M91556       ER------SKHLKNGCRRGSSLCQISCASKKGKIWQNIRKTCCKIVENNWFKCFIGLVTL 945
                             .   :.: * :         :.     .      :*::*  ***:.**: ** :: *

                    >>>>>>>>                <<<<<<< III-S2 >>>>>>>>>>>      <<<<<<<
hSCN1A              LSSGALAFEDIYIDQRKTIKTMLEYADKVFTYIFILEMLLKWVAYGYQTYFTNAWCWLDF 1289
hSCN5A-M77235       LSSGALAFEDIYLEERKTIKVLLEYADKMFTYVFVLEMLLKWVAYGFKKYFTNAWCWLDF 1276
hSCN10A-AF117907    LSSGSLAFEDYYLDQKPTVKALLEYTDRVFTFIFVFEMLLKWVAYGFKKYFTNAWCWLDF 1223
hSCN4A-M81758       LSSGALAFEDIYIEQRRVIRTILEYADKVFTYIFIMEMLLKWVAYGFKVYFTNAWCWLDF 1102
hSCN2A              LSSGALAFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLKWVAYGFQVYFTNAWCWLDF 1279
hSCN3A              LSSGALAFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLKWVAYGFQTYFTNAWCWLDF 1228
hSCN8A-AB027567     LSSGALAFEDIYIEQRKTIKTILEYADKVFTYIFILEMLLKWTAYGFVKFFTNAWCWLDF 1269
hSCN9A-X82835       LSSGALAFEDIYIERKKTIKIILEYADKIFTYIFILEMLLKWIAYGYKTYFTNAWCWLDF 1263
hSCN6A-M91556       LSTGTLAFEDIYIDQRKTIKILLEYADMIFTYIFILEMLLKWMAYGFKAYFSNGWYKLDF 1005
                    **:*:***** *::.: .:: :***:* ;**::*::****** ***:   ;*:* *  ***
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                      III-S3 >>>>>>>>>    <<<<<< III-S4 >>>>>>>>>
hSCN1A                LIVDVSLVSLTANALGYSELGAIKSLRTLRALRPLRALSRFEGMRVVVNALLGAIPSIMN 1349
hSCN5A-M77235         LIVDVSLVSLVANTLGFAEMGPIKSLRTLRALRPLRALSRFEGMRVVVNALVGAIPSIMN 1336
hSCN10A-AF117907      LIVNISLISLTAKILEYSEVAPIKALRTLRALRPLRALSRFEGMRVVVDALVGAIPSIMN 1283
hSCN4A-M81758         LIVDVSIIGLVANWLGYSELGPIKSLRTLRALRPLRALSRFEGMRVVVNALIGAIPSIMN 1162
hSCN2A                LIVDVSLVSLTANALGYSELGAIKSLRTLRALRPLRALSRFEGMRAVVNALLGAIPSIMN 1339
hSCN3A                LIVDVSLVSLVANALGYSELGAIKSLRTLRALRPLRALSRFEGMRVVVNALVGAIPSIMN 1288
hSCN8A-AB027567       LIVAVSLVSLIANALGYSELGAIKSLRTLRALRPLRALSRFEGMRVVVNALVGAIPSIMN 1329
hSCN9A-X82835         LIVDVSLVTLVANTLGYSDLGPIKSLRTLRALRPLRALSRFEGMRVVVNALIGAIPSIMN 1323
hSCN6A-M91556         VVVIVFCLSLIGKTR-----EELKPLISMKFLRPLRVLSQFERMKVVVRALIKTTLPTLN 1060
                      ::* :  ::* .:       :  :*.* ::: *****.**:** *:.** **: :  . :*

                      <<<<<< III-S5 >>>>>>>>>
hSCN1A                VLLVCLIFWLIFSIMGVNLFAGKFYHCINTTTG--DRFDIEDVNNHTDCLKLIE-RNETA 1406
hSCN5A-M77235         VLLVCLIFWLIFSIMGVNLFAGKFGRCINQTEGDLPLN-YTIVNNKSQCESLNL--TGEL 1393
hSCN10A-AF117907      VLLVCLIFWLIFSIMGVNLFAGKFWRCINYTDGEFSLVPLSIVNNKSDCKIQNS--TGSF 1341
hSCN4A-M81758         VLLVCLIFWLIFSIMGVNLFAGKFYYCINTTT--SERFDISEVNNKSECESLMH--TGQV 1218
hSCN2A                VLLVCLIFWLIFSIMGVNLFAGKFYHCINYTTG--EMFDVSVVNNYSECKALIE-SNQTA 1396
hSCN3A                VLLVCLIFWLIFSIMGVNLFAGKFYHCVNMTTG--NMFDISDVNNLSDCQALG----KQA 1342
hSCN8A-AB027567       VLLVCLIFWLIFSIMGVNLFAGKYHYCFNETSE--IRFEIEDVNNKTECEKLMEGNNTEI 1387
hSCN9A-X82835         VLLVCLIFWLIFSIMGVNLFAGKFYECINTTDG--SRFPASQVPNRSECFALMN-VSQNV 1380
hSCN6A-M91556         VFLVCLMIWLIFSIMGVDLFAGKFYECIDPTSG--ERFPSSEVMNKSRCESLLF--NESM 1116
                      *:****::*********:****::  *.: *            * * : *

                                                                      <<<<<<<<<<
hSCN1A                FWKNVKVNFDNVGFGYLSLLQVATFKGWMDIMYAAVDSRNVELQPKYEESLYMYLYFVIF 1466
hSCN5A-M77235         YWTKVKVNFDNVGAGYLALLQVATFKGWMDIMYAAVDSRGYEEQPQWEYNLYMYIYFVIF 1453
hSCN10A-AF117907      FWVNVKVNFDNVAMGYLALLQVATFKGWMDIMYAAVDSREVNMQPKWEDNVYMYLYFVIF 1401
hSCN4A-M81758         FWLNVKVNYDNVGLGYLSLLQVATFKGWMDIMYAAVDSREKEEQPQYEVNLYMYLYFVIF 1278
hSCN2A                FWKNVKVNFDNVGLGYLSLLQVATFKGWMDIMYAAVDSRNVELQPKYEDNLYMYLYFVIF 1456
hSCN3A                FWKNVKVNFDNVGAGYLALLQVATFKGWMDIMYAAVDSRDVKLQPVYEENLYMYLYFVIF 1402
hSCN8A-AB027567       FWKNVKINFDNVGAGYLALLQVATFKGWMDIMYAAVDSRKPDEQPKYEDNIYMYIYFVIF 1447
hSCN9A-X82835         FWKNLKVNFDNVGLGYLSLLQVATFKGWTIIMYAAVDSVNVDKQPKYEYSLYMYIYFVVF 1440
hSCN6A-M91556         FWENAKMNIDNVGNGFLSLLQVATFNGWITIMNSAIDSVAVNIQPHFEVNIYMYCYFINF 1176
                       * : *:*:***. *:*:*******:**  ** :*:**    . ** :* .:*** **: *

                      III-S6 >>>>>>>>>>
hSCN1A                IIFGSFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1526
hSCN5A-M77235         IIFGSFFTLNLFIGVIIDNFNQQKKKLGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1513
hSCN10A-AF117907      IIFGGFFTLNLFVGVIIDNFNQQKKKLGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1461
hSCN4A-M81758         IIFGSFFTLNLFIGVIIDNFNQQKKKLGGKDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1338
hSCN2A                IIFGSFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1516
hSCN3A                IIFGSFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1462
hSCN8A-AB027567       IIFGSFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1507
hSCN9A-X82835         IIFGSFFTLNLFIGVIIDNFNQQKKKLGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRP 1500
hSCN6A-M91556         IIFGVFLPLSMLITVIIDNFNKHKIKLGGSNIFITVKQRKQYRRLKKLMYEDSQRPVPRP 1236
                      **** *:.*.::: *******::* *:**.:**:* :*:* *. :***  :..*:*:***

                                 <<<<<<< IV-S1 >>>>>>>>>>          <<<<< IV-S2 >>>
hSCN1A                GNKFQGMVFDFVTRQVFDISIMILICLNMVTMMVETDDQSEYVTTILSRINLVFIVLFTG 1586
hSCN5A-M77235         LNKYQGFIFDIVTKQAFDVTIMFLICLNMVTMMVETDDQSPEKINILAKINLLFVAIFTG 1573
hSCN10A-AF117907      LNKFQGFVFDIVTRQAFDITIMVLICLNMITMMVETDDQSEEKTKILGKINQFFVAVFTG 1521
hSCN4A-M81758         QNKIQGMVYDLVTKQAFDITIMILICLNMVTMMVETDDQSQLKVDILYNINMIFIIIFTG 1398
hSCN2A                ANKFQGMVFDFVTKQVFDISIMILICLNMVTMMVETDDQSQEMTNILYWINLVFIVLFTG 1576
hSCN3A                ANKFQGMVFDFVTRQVFDISIMILICLNMVTMMVETDDQGKYMTLVLSRINLVFIVLFTG 1522
hSCN8A-AB027567       LNKIQGIVFDFVTQQAFDIVIMMLICLNMVTMMVETDTQSKQMENILYWINLVFVIFFTG 1567
hSCN9A-X82835         GNKIQGCIFDLVTNQAFDISIMVLICLNMVTMMVEKEGQSQHMTEVLYWINVVFIILFTG 1560
hSCN6A-M91556         LNKLQGFIFDVVTSQAFNVIVMVLICFQAIAMMIDTDVQSLQMSIALYWINSIFVMLYTM 1296
                       ** ** ::*.** *.*:: :*.***:: ::**::.: *.      *  ** .*: .:*

                      >>>>>>>>>       <<<<<<<< IV-S3 >>>>>>>>>          <<<<<<<<<
hSCN1A                ECVLKLISLRHYYFTIGWNIFDFVVVILSIVGMFLAELIE--KYFVSPTLFRVIRLARIG 1644
hSCN5A-M77235         ECIVKLAALRHYYFTNSWNIFDFVVVILSIVGTVLSDIIQ--KYFFSPTLFRVIRLARIG 1631
hSCN10A-AF117907      ECVMKMFALRQYYFTNGWNVFDFIVVVLSIASLIFSAILKSLQSYFSPTLFRVIRLARIG 1581
hSCN4A-M81758         ECVLKMLALRQYYFTVGWNIFDFVVVILSIVGLALSDLIQ--KYFVSPTLFRVIRLARIG 1456
hSCN2A                ECVLKLISLRYYYFTIGWNIFDFVVVILSIVGMFLAELIE--KYFVSPTLFRVIRLARIG 1634
hSCN3A                EFVLKLVSLRHYYFTIGWNIFDFVVVILSIVGMFLAEMIE--KYFVSPTLFRVIRLARIG 1580
hSCN8A-AB027567       ECVLKMFALRHYYFTIGWNIFDFVVVILSIVGMFLADIIE--KYFVSPTLFRVIRLARIG 1625
hSCN9A-X82835         ECVLKLISLRHYYFTVGWNIFDFVVVIISIVGMFLADLIE--TYFVSPTLFRVIRLARIG 1618
hSCN6A-M91556         ECILKMIAFRCFYFTIAWNIFDFMVVIFSITGLCLPMTVG--SYLVPPSLVQLILLSRII 1354
                      * ::*: ::* :*** .**:***:**::**..  :.  :        ..*:*.::* *:**
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                     IV-S4 >>>>>>>                  <<<<<<< IV-S5 >>>>>>>>>
hSCN1A               RILRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYAIFGMSNFAYVKREVGIDDM 1704
hSCN5A-M77235        RILRLIRGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYSIFGMANFAYVKWEAGIDDM 1691
hSCN10A-AF117907     RILRLIRAAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYSIFGMSSFPHVRWEAGIDDM 1641
hSCN4A-M81758        RVLRLIRGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYSIFGMSNFAYVKKESGIDDM 1516
hSCN2A               RIIRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYAIFGMSNFAYVKREVGIDDM 1694
hSCN3A               RIIRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYAIFGMSNFAYVKKEAGIDDM 1640
hSCN8A-AB027567      RIIRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIFSIFGMSNFAYVKHEAGIDDM 1685
hSCN9A-X82835        RILRLVKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIYAIFGMSNFAYVKKEDGINDM 1678
hSCN6A-M91556        HMLRLGKGPKVFHNLMLPLMLSLPALLNIILLIFLVMFIYAVFGMYNFAYVKKEAGINDV 1414
                     ::*** :..* ::.*::.**:*****:** **:******:::*** .*.:*: * **:*:

                                                                               <<
hSCN1A               FNFETFGNSMICLFQITTSAGWDGLLAPILNSKPPDCDPNKVNPGSSVKGDCGNPSVGIF 1764
hSCN5A-M77235        FNFQTFANSMLCLFQITTSAGWDGLLSPILNTGPPYCDPTLPNS-NGSRGDCGSPAVGIL 1750
hSCN10A-AF117907     FNFQTFANSMLCLFQITTSAGWDGLLSPILNTGPPYCDPNLPNS-NGTRGDCGSPAVGII 1700
hSCN4A-M81758        FNFETFGNSIICLFEITTSAGWDGLLNPILNSGPPDCDPNLENPGTSVKGDCGNPSIGIC 1576
hSCN2A               FNFETFGNSMICLFQITTSAGWDGLLAPILNSGPPDCDPDKDHPGSSVKGDCGNPSVGIF 1754
hSCN3A               FNFETFGNSMICLFQITTSAGWDGLLAPILNSAPPDCDPDTIHPGSSVKGDCGNPSVGIF 1700
hSCN8A-AB027567      FNFETFGNSMICLFQITTSAGWDGLLLPILN-RPPDCSLDKEHPGSGFKGDCGNPSVGIF 1744
hSCN9A-X82835        FNFETFGNSMICLFQITTSAGWDGLLAPILNSKPPDCDPKKVHPGSSVEGDCGNPSVGIF 1738
hSCN6A-M91556        SNFETFGNSMLCLFQVAIFAGWDGMLDAIFNSKWSDCDPDKINPGTQVRGDCGNPSVGIF 1474
                      **:**.**::***:::  *****:* .*:*    . *.      :. .  .****.*::**

                              #Ser1773Tyr in SCN1A
                     <<< IV-S6 >>>>>>>>>>>>
hSCN1A               FFVSYIIISFLVVVNMYIAVILENFSVATEESAEPLSEDDFEMFYEVWEKFDPDATQFME 1824
hSCN5A-M77235        FFTTYIIISFLIVVNMYIAIILENFSVATEESTEPLSEDDFDMFYEIWEKFDPEATQFIE 1810
hSCN10A-AF117907     FFTTYIIISFLIVVNMYIAVILENFNVATEESTEPLSEDDFDMFYETWEKFDPEATQFIT 1760
hSCN4A-M81758        FFCSYIIISFLIVVNMYIAIILENFNVATEESSEPLGEDDFEMFYETWEKFDPDATQFIA 1636
hSCN2A               FFVSYIIISFLVVVNMYIAVILENFSVATEESAEPLSEDDFEMFYEVWEKFDPDATQFIE 1814
hSCN3A               FFVSYIIISFLVVVNMYIAVILENFSVATEESAEPLSEDDFEMFYEVWEKFDPDATQFIE 1760
hSCN8A-AB027567      FFVSYIIISFLIVVNMYIAIILENFSVATEESADPLSEDDFETFYEIWEKFDPDATQFIE 1804
hSCN9A-X82835        YFVSYIIISFLVVVNMYIAVILENFSVATEESTEPLSEDDFEMFYEVWEKFDPDATQFIE 1798
hSCN6A-M91556        YFVSYILISWLIIVNMYIVVVMEFLNIASKKKNKTLSEDDFRKFFQVWKRFDPDRTQYID 1534
                     :* :**:**:*::** **.:::* :.:*:::. ..*.****  *:: *::***: **::

hSCN1A               FEKLSQFAAALEPPLNLPQPNKLQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGEMDA 1884
hSCN5A-M77235        YSVLSDFADALSEPLRIAKPNQISLINMDLPMVSGDRIHCMDILFAFTKRVLGESGEMDA 1870
hSCN10A-AF117907     FSALSDFADTLSGPLRIPKPNRNILIQMDLPLVPGDKIHCLDILFAFTKNVLGESGELDS 1820
hSCN4A-M81758        YSRLSDFVDTLQEPLRIAKPNKIKLITLDLPMVPGDKIHCLDILFALTKEVLGDSGEMDA 1696
hSCN2A               FAKLSDFADALDPPLLIAKPNKVQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGEMDA 1874
hSCN3A               FSKLSDFAAALDPPLLIAKPNKVQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGEMDA 1820
hSCN8A-AB027567      YCKLADFADALEHPLRVPKPNTIELIAMDLPMVSGDRIHCLDILFAFTKRVLGDSGELDI 1864
hSCN9A-X82835        FSKLSDFAAALDPPLLIAKPNKVQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGEMDS 1858
hSCN6A-M91556        SSKLSDFAAALDPPLFMAKPNKGQLIALDLPMAVGDRIHCLDILLAFTKRVMGQDVRMEK 1594
                         *::*. :*. ** :.:**   ** :***:. **:***:***:*:**.*:*:. .::

hSCN1A               LRIQMEERFMASNPSKVSYQPITTTLKRKQEEVSAVIIQRAYRRHLLKRTVKQASFTYNK 1944
hSCN5A-M77235        LKIQMEEKFMAANPSKISYEPITTTLRRKHEEVSAMVIQRAFRRHLLQRSLKHASFLFRQ 1930
hSCN10A-AF117907     LKANMEEKFMATNLSKSSYEPIATTLRWKQEDISATVIQKAYRSYVLHRSMALSNTPCVP 1880
hSCN4A-M81758        LKQTMEEKFMAANPSKVSYEPITTTLKRKHEEVCAIKIQRAYRRHLLQRSMKQASYMYRH 1756
hSCN2A               LRIQMEERFMASNPSKVSYEPITTTLKRKQEEVSAIIIQRAYRRYLLKQKVKKVSSIYKK 1934
hSCN3A               LRIQMEDRFMASNPSKVSYEPITTTLKRKQEEVSAAIIQRNFRCYLLKQRLKNISSNYNK 1880
hSCN8A-AB027567      LRQQMEERFVASNPSKVSYEPITTTLRRKQEEVSAVVLQRAYRGHLARRGFICKKTTSNK 1924
hSCN9A-X82835        LRSQMEERFMSANPSKVSYEPITTTLKRKQEDVSATVIQRAYRRYRLRQNVKNISSIYIK 1918
hSCN6A-M91556        VVSEIESGFLLANPFKITCEPITTTLKRKQEAVSATIIQRAYKNYRLRRNDKNTSDIHMI 1654
                     :    :*. *: :*  * : :**:***: *:* :.*  :*: :: :  ::       .

hSCN1A               NKI--KGGANLLIKEDMIIDRINENSITEK---TDLTMSTAACPPSYDRVTKPIVEK--- 1996
hSCN5A-M77235        QAGSGLSEEDAPEREGLIAYVMSENFSRPLGPPSSSSISSTSFPPSYDSVTRATSDNLQV 1990
hSCN10A-AF117907     RA---EEEAASLPDEGFVAFTANENCVLPD---KSETASATSFPPSYESVTRGLSDRVNM 1934
hSCN4A-M81758        SHD--GSGDDAPEKEGLLANTMSKMYGHEN----GNSSSPSPEEKGEACDAGPTMGLMPI 1810
hSCN2A               DKG--KECDGTPIKEDTLIDKLNENSTPEK---TDMTPSTTS-PPSYDSVTKPEKEK--- 1985
hSCN3A               EAI--KGRIDLPIKQDMIIDKLNGNSTPEK---TDGSSSTTS-PPSYDSVTKPDKEK--- 1931
hSCN8A-AB027567      LE-------------------NGGTHREK---KESTPSTAS-LPSYDSVTKPEKEKQQR 1960
hSCN9A-X82835        DGD--RD-DDLLNKKDMAFDNVNENSSPEK---TDATSSTTS-PPSYDSVTKPDKEK--- 1968
hSCN6A-M91556        DGD-------------------------------RDVHATKEGAYPDKAK--------- 1673
                                                       .:
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hSCN1A          HEQECNDEKAFGK---------- 2009
hSCN5A-M77235   kGGDYSHSEDLADFPPSPDFDRESIV 2016
hSCN10A-AF117907 RTSSSIQNEDEATSKELIAFGP---- 1956
hSCN4A-M81758   SPSDIAWPAFPPGQTVKPGVKESLV 1836
hSCN2A          PEKDWSEKEDVGKDIREEKK------ 2005
hSCN3A          PEKDKPEVESKGKEVPENQK------ 1951
hSCN8A-AB027567 AEEGKEEKAKFQKEVPESKC------ 1980
hSCN9A-X82835   YEQDETEKEDKGKDSKESIK------ 1988
hSCN6A-M91556   -EKSPTQSQI---------------- 1682
                                    ::
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Description of the protein sequences used in the alignment:

SCN1A: sequence determined by Lafreniere, Rouleau & Rochefort **(this application)**

SCN2A: sequence determined by Lafreniere, Rouleau & Rochefort **(this application)**

SCN3A: sequence determined by Lafreniere, Rouleau & Rochefort **(this application)**

SCN4A: from M81758 deposited to GenBank on **13-JAN-1995** by George,A.L. Jr., Komisarof,J., Kallen,R.G. and Barchi,R.L. Primary structure of the adult human skeletal muscle voltage-dependent sodium channel Ann. Neurol. 31 (2), 131-137 (1992)

SCN5A: from M77235 deposited to GenBank on **31-DEC-1994** by Gellens,M.E., George,A.L. Jr., Chen,L.Q., Chahine,M., Horn,R., Barchi,R.L. and Kallen,R.G. Primary structure and functional expression of the human cardiac tetrodotoxin-insensitive voltage-dependent sodium channel Proc. Natl. Acad. Sci. U.S.A. 89 (2), 554-558 (1992)

SCN6A: from M91556 deposited to GenBank on **07-JAN-1995** by George,A.L. Jr., Knittle,T.J. and Tamkun,M.M. Molecular cloning of an atypical voltage-gated sodium channel expressed in human heart and uterus: evidence for a distinct gene family Proc. Natl. Acad. Sci. U.S.A. 89 (11), 4893-4897 (1992)

SCN8A: from AB027567 deposited to GenBank on **01-JUN-1999** by Lin,C., Numakura,C. and Kiyoshi,H. cDNA sequnce of human sodium channel, SCN8A(Unpublished)

SCN9A: from X82835 deposited to GenBank on **21-NOV-1994** by Klugbauer,N., Lacinova,L., Flockerzi,V. and Hofmann,F. Structure and functional expression of a new member of the tetrodotoxin-sensitive voltage-activated sodium channel family from human neuroendocrine cells EMBO J. 14 (6), 1084-1090 (1995)

SCN10A: from AF117907 deposited to GenBank on **18-MAY-1999** by Rabert,D.K., Koch,B.D., Ilnicka,M., Obernolte,R.A., Naylor,S.L., Herman,R.C., Eglen,R.M., Hunter,J.C. and Sangameswaran,L. A tetrodotoxin-resistant voltage-gated sodium channel from human dorsal root ganglia, hPN3/SCN10A. Pain 78 (2), 107-114 (1998)